INVESTIGATING THE LOSS OF CRYSTAL STRUCTURE IN CARBOHYDRATE MATERIALS

BY

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DISSERTATION

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ABSTRACT

Twenty-five carbohydrate type materials were screened using differential scanning calorimetry (DSC) to characterize the heating rate dependence of their melting temperature. Three heating rates were used: 1, 5 and 25°C/min. Based on previous research, it was hypothesized that if the material had the same melting onset temperature (Tm onset) regardless of heating rate, the material was classified as a thermodynamic melting material. Five compounds (erythitol, maltitol, mannitol, sorbitol and xylitol) exhibited little to no change in Tm onset regardless of heating rate and were classified in the no/low heating rate dependency group. The eleven compounds (D and L arabinose, fructose, glucose anhydrous, glucose monohydrate, lactose anhydrous, lactose monohydrate, maltose, sucrose, trehalose and xylose) that exhibited a very large difference in Tm onset (greater than 10°C) between the lowest (1°C/min) and highest heating rate (25°C/min) were classified in the high heating rate dependency group and were considered to be apparent melting materials. The remaining compounds (citric acid, galactose, lactitol, lactulose, mannose, raffinose, ribose, and tagatose) exhibited a Tm onset difference of 2 to 10°C between the lowest and highest heating rates and were classified in the medium heating rate dependency group. Further investigation of the materials in the medium heating rate dependency group will need to be done in order to understand more conclusively their thermal behavior and to determine if they are apparent melting or thermodynamic melting materials. A shift in peak onset temperature with heating rate is a function of the activation energy of the process causing the shift. Therefore, each material can show a different shift. High activation energy results in a small shift, while low activation energy results in a large shift.

D and L arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, ribose, xylose, xylitol and citric acid were tested to understand their thermal behavior using regular modulated differential scanning calorimetry (MDSC), quasi-isothermal MDSC and TGA. Using regular MSDC did not yield any meaningful signals outside of total heat flow. The equations used to calculate the regular MDSC signals could not be applied during the loss in crystal structure event, since the modulated heating rate cannot be controlled during the loss of crystal structure. The quasi-isothermal MDSC yielded important information in regards to the reversing heat capacity (Cp) signal. If the reversing Cp signal exhibited signs of recrystallization during melting and returned to the baseline at the end of the heating process, the material exhibited thermodynamic melting. If it did not, the material was could be explained to be apparent melting. An overlay of plots for Tm onset from DSC and Ti (onset of initial

decomposition) from TGA showed that several compounds (L- arabinose, D- arabinose and galactose) exhibited a loss in weight that occurred before the onset of the loss in crystalline structure, even without taking thermal lag into consideration. Glucose monohydrate exhibited weight loss that occurs substantially before the onset of the loss of crystalline structure, but the early weight loss is attributed to the loss in hydrate water. Fructose loss of crystalline structure and onset of decomposition overlay showed both events occurring at a similar temperature. Xylose and ribose overlay weight loss occurred at a time slightly after the onset the loss of crystalline structure. In the case of ribose, Tm onset occurs under 100°C, and weight loss would not occur until after 100°C when the water is volatile. The onset of decomposition occurred significantly after the loss of crystalline structure in xylitol. The citric acid Tm onset occurred before the Ti. The difference between Tm onset from DSC and the Ti from TGA were similar numerically for the sugars and citric acid (<15°C), but very different for the polyol, xylitol (~125°C). Through comparison of Tm onset to Ti and through reversing Cp results from Quasi-isothermal MDSC, L- and D- arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, ribose, and xylose were found to be apparent melting materials, whereas xylitol was found to be a thermodynamic melting material. The results on citric acid were inconclusive.

Fructose, galactose, glucose monohydrate, sucrose and xylose were each held at a temperature below their measured Tm onset value for various times. Visual inspection of the samples, reversing heat capacity (Cp), monosaccharides retention and the HMF and furfural of each sample were measured. Sugar retention was measured by HPLC. HMF and furfural were selected as decomposition indicator compounds and were detected by HPLC. Each of the sugars tested showed an increase in reversing Cp, a development of a yellow color within the sugar crystal, a decrease in the amount of sugar present, and an increase in HMF and furfural with increasing time at the isothermal temperature. The sugars showed the decomposition indicator compound (HMF or furfural) being identified after 20% of the stabilization of heat capacity in all cases. Each of these factors (visual appearance, reversing Cp, decomposition products) indicate decomposition occurs below the measured melting temperature, and the loss of crystalline structure is caused by the onset of thermal decomposition. Xylitol was held at its melting temperature (94°C) for 1000, 2000, and 3000 minutes. Holding xylitol at 94°C did not show any change in heat capacity, or loss in xylitol during any of the three holding times. Decomposition products were not detected validating that xylitol did not decompose.

When comparing the apparent melting materials (xylose, glucose, fructose, sucrose, and galactose) to related thermodynamic materials (mannitol and xylitol), the major structural difference is the

presence of a carbonyl group (aldehydes or ketones) compared to a hydroxyl group. Citric acid also contains a carbonyl group in the form of carboxylic acid, but the results for citric acid were inconclusive. The polyols (xylitol) have been reduced and only contain hydroxyl groups. The polyols were demonstrated to be thermodynamic melting materials.

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CHAPTER 1

Introduction

Rationale and Significance

An understanding of the mechanism underlying the loss of crystalline structure during heating of sugars is of fundamental importance to the food and pharmaceutical industries. Many processes involve heating, and understanding how ingredients may react during heating will help predict processing outcomes and finished product qualities and stability. Depending on the processing and finished product attributes needed in food and pharmaceutical systems, different sugars are used. There has also been a recent increase in the use of rare sugars (e.g. ribose and allulose) as a natural alternative to traditional sucrose in food products. The rare sugars provide calorie reduction with similar functionality. Understanding how these sugars behave thermally will aid in their use.

Melting has traditionally been considered a fundamental property in the characterization of compounds. Investigating the loss of crystalline structure of sugars and related carbohydrates is usually performed by Differential Scanning Calorimetry (DSC). Observation of the thermal behavior during heating provides an indication of the compound's processing tolerance and predicts behavior as compounds go through food or pharmaceutical processes.

There has long been information on the melting and decomposition of sugars occurring during the range of melting temperatures. The explanation given by Lee et al. (2011) of apparent melting is a significant change in the understanding of how and why some sugars lose their crystalline structure. Further work is needed to determine if apparent melting exists only for the compounds studied by Lee et al. (2011a) – fructose, glucose and sucrose, or if it occurs in other materials as well. As more materials are explored, a pattern for predicting when a material may exhibit apparent melting and which materials may exhibit thermodynamic melting can be established. With this further understanding, these sugars and other related materials can be used more effectively in food and pharmaceutical applications.

The primary aim of this research was to expand the understanding of apparent melting materials, first to screen a large number of compounds to observe their thermal behavior, then to further investigate any compounds which exhibit possible apparent melting behavior. Understanding the thermal behavior will allow the industry to apply the new paradigm of apparent melting beyond its initial scope. It will also help to form a framework for predicting thermodynamic or apparent melting behavior during heating of materials. Apparent melting is a kinetic process, which means that it is time

and temperature dependent. Under non-isothermal conditions, the faster the heating rate, the higher the onset temperature will be. Under isothermal (or constant temperature) conditions, when the isothermal temperature is close to the melting temperature, materials will decompose in a shorter time compared to materials held at a temperature much lower than the melting temperature. Materials held at a lower temperature will decompose in a much longer time. Information on how various sugars and related compounds melt can guide new sugar and sugar alcohol based product development in both the food and pharmaceutical industries. As this understanding of thermal behavior is taken to broader application, patterns will develop in the structure of compounds that will help predict mechanisms or causes of apparent melting materials.

Statement of Research Objectives

Original research from Lee et al. (2011a) introduced the concept of apparent melting in sucrose, fructose and glucose. The purpose of the current research is to investigate similar carbohydrate compounds to determine their melting behavior. The materials studied will include additional sugars, polyols, and citric acid. Testing additional sugars will determine if the heating rate dependence is found only in sucrose, fructose and glucose, or if it applies to other sugars as well. Testing additional polyols again tests similar numbers of carbons and functional groups, but the polyols are completely reduced, having only hydroxyl functional groups and no carbonyl groups. Citric acid tests a material with similar carbon number and functional groups as the sugars, but the carboxylic acid has the carbonyl group and the hydroxyl group on the same (terminal) carbon.

Melting has been described as a thermodynamic event that occurs at a single, time-independent (i.e., heating rate independent) temperature with a constant enthalpy value (ΔH), where the crystalline solid and corresponding liquid phases are in thermodynamic equilibrium ($\Delta G=0$) at a constant pressure (Wunderlich, 1990). Using the Wunderlich definition for guidance, the melting parameters ($T_{m\ onset}$, $T_{m\ peak}$, and ΔH) for various carbohydrates will be investigated to allow the comparison of melting behavior to the traditional definition of thermodynamic melting.

Therefore, the ultimate objective of this research is to expand the understanding of the fundamental mechanism underlying the loss of crystalline structure (melting) in various carbohydrate compounds and to understand and predict why some materials exhibit thermodynamic melting characteristics and some materials exhibit apparent melting.

OBJECTIVE 1: Screen various crystalline materials and classify their melting behavior as heating rate dependent (apparent melting) or heating rate independent (thermodynamic melting) as determined by DSC. Hypothesis: All sugars are apparent melting, all polyols are thermodynamic melting.

OBJECTIVE 2: Identify methods that can be used to further classify and differentiate apparent melting materials. Hypothesis: Quasi-isothermal MDSC and TGA together can be predictive. Materials in the medium heating rate dependence group will be apparent melting.

OBJECTIVE 3: Detection of decomposition components and loss in crystal structure in fructose, glucose, galactose and xylose held isothermally by quasi-isothermal modulated DSC. Hypothesis: Decomposition components will be detected at temperatures under the onset of the loss in crystal structure.

References

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CHAPTER 2

Literature Review

Importance of Sugar

Sugar is a small, relatively simple molecule, but is one of the most powerful building blocks in nature. Sugar, in various forms, is used by plants and animals for energy: both to store energy and as a source of energy. Sucrose is generated in the leaves of plants by photosynthesis, where carbon dioxide from the air is combined with water drawn through the roots to form sugars (Nicol, 1991). The sugar is either used right away or stored in stalks, leaves, tubers and seeds for future use by the plant.

In the food and pharmaceutical industries, sugars achieve their importance primarily by imparting sweetness to products, but also by contributing to structure and texture. The desirable qualities contributed by sugars are numerous, and include sweetening, bulking, texturizing, adding viscosity and acting as carriers for active pharmaceutical ingredients (El Khadem, 1988). Confections are a class of food entirely based on sugars, mainly sucrose, which drive and control the eating qualities. Sugars contribute to the browning and texture of baked products. In dairy products, sugars sweeten, add solids and increase mouth feel. In jams and jellies, the high sugar content actually acts as a preservative and controls the setting of the pectin. In breakfast cereals, sugars are used as a coating, which increases the bowl life and adds to the flavor of the cereal (Nicol, 1991). With sugar's broad application and functionality, it is crucial to the food, beverage and pharmaceutical industries.

Recently, sugar in the American diet has been under fire, and companies have striven to reduce the grams of sugar present in foods as shown on the nutrition facts label (Jargon, 2011; Taubes, 2011; Welsh et al., 2011). Sugar alcohols or sugar substitutes have been used to contribute to the sweetness and structure of foods and pharmaceuticals, but with decreased calorie content (Billaux et al., 1991). The food ingredient industry has begun to introduce "rare" sugars, such as ribose, tagatose and allulose, which are natural occurring, but contain fewer calories and still impart many of sugar's unique functional properties.

Sugars, sugar alcohols and other related carbohydrates are important in living plants and animals as an energy source. In food and pharmaceutical processing, these materials are essential to develop the desired finished eating qualities expected in the products consumers enjoy. The industry's ability to optimize the use of sugars, sugar alcohols, and other related carbohydrates will be expanded by further study of the impact of the heating process.

Overview of Sugar Chemistry

The simplest form of a sugar is a monosaccharide. A monosaccharide consists of a carbon backbone with a carboxyl group and many hydroxyl groups. In nature, sugars can be the straight chain form, but are frequently found in a ring structure (Hindsgaul, 1999). Each of the monosaccharides varies only slightly in the placement of the different hydroxyl groups in the ring structure. For instance, ribose, arabinose and xylose, pictured in Figure 2-1, are all 5-carbon sugars. The carbons in ribose were labeled in Figure 2-1 according to standard numbering convention, which starts from the most important end carbon and continues in order of the next connecting carbon. The position of the hydroxyl groups on each carbon differentiates the sugars. For example, ribose and arabinose have the same structure with the exception of the hydroxyl group on the number two carbon; ribose has the hydroxyl group in the down positon compared to arabinose that has the hydroxyl in the up position. Further comparison shows xylose and ribose have the same configuration of the number two carbon, but differ on the number three carbon. In ribose, the number three carbon occurs on the hydroxyl group in the down position, but on xylose in the up position (El Khadem, 1988).

Fructose, glucose and galactose are three 6-carbon sugars, which are the fundamental building blocks in human biochemistry. Glucose is the sugar used to carry energy in the blood. Fructose is found naturally in fruits and is part of glycolysis in human metabolism (as fructose-6-phosphatase) (Hyvonen and Koivistoinen, 1982). Galactose is a sugar also found in the human body in glycolipids and glycoproteins. It is also one of the two sugars that compose lactose, or milk sugar. These three 6-carbon sugars are similar, having the same molecular formula, but differ slightly in their configuration. Because of their importance and prevalence in human metabolism and food, these three sugars will be considered in this study.

Of the eight possible D- and L-aldopentoses, only four occur naturally, namely D-xylose, D-ribose, and D- and L-arabinose. These are mostly present naturally as constituents of polysaccharides. Of the eight aldo-D-hexoses possible, only D-glucose occurs abundantly. Ketoses also occur in the free-state, but only D-fructose occurs to any great extent (Shallenburger and Birch, 1975).

Two monosaccharides can be linked together to form disaccharides. Different monosaccharides and different linkages can form different disaccharides. Table 2-1summarizes these disaccharide relationships among glucose, fructose and galactose. For example, galactose and glucose can combine to form either lactose or melibiose, and fructose and glucose can form sucrose. Trisaccharides are a

combination of three monosaccharides; for example, raffinose is a combination of fructose, glucose and galactose (El Khadem, 1988).

A sugar alcohol (also referred to as a polyol) is a hydrogenated form of a carbohydrate (be it a simple sugar or more complex carbohydrate). The carbonyl (be it an aldehyde or a ketone) is reduced (or hydrogenated) to form a hydroxyl group (El Khadem, 1988).

Table 2-2 shows common mono- and di-saccharides and their corresponding sugar alcohols. The hydroxyl group formation results in several modifications in the molecule. Most obviously there are the chemical changes, but these lead to functional changes in the food, as well as metabolic changes in the human or animal eating the food. Chemically, the carbohydrate no longer has an active carbonyl group, which prevents it from being a reducing sugar, and it can no longer form a ring structure in solution. The loss of the carbonyl group affects the browning ability and solubility, and frequently produces a negative heat of solution causing a cooling sensation in the mouth. Metabolically, sugar alcohols are not completely digested, which gives a reduction in calories per gram versus the original carbohydrate of 4 kcals/gram (Billaux et al., 1991).

Melting Temperature and Decomposition

Melting temperature has long been a basic parameter used for characterizing compounds (Wunderlich, 1990). Melting is commonly defined as the loss of crystalline structure, or the transition between a liquid and a solid. In the past, the melting temperature has been considered a unique and repeatable event, which has allowed it to be used for identification purposes. In general chemistry class, students are taught to use a simple device that heats a compound slowly in a capillary tube to determine the material's melting point. Students observe the loss of crystallinity of the compound in the capillary tube, witnessing the transition from a solid to a liquid. The melting temperature is recorded as a fundamental characteristic of the crystalline compounds. Students use the measurement of loss of crystalline structure in a capillary tube to identify the unknown compound in the tube.

Melting temperature can be measured more precisely using techniques such as DSC, which uniformly heats the sample and records the difference in heat absorption versus a reference, usually an empty pan. Samples undergoing a thermal event (such as melting) will have different heat absorption than the reference, which can be recorded. Thermal events can be endothermic (absorbing heat) or exothermic (giving off heat). Because the crystals require energy to transition from the solid to the liquid state, melting is an endothermic event. Energy is required to disrupt the intermolecular hydrogen

bonding, moving to a state of increased entropy. DSC measures three melting parameters, the onset melting temperature ($T_{m\ onset}$ in °C), the peak melting temperature ($T_{m\ peak}$ in °C), and the melting enthalpy (ΔH in J/g). Figure 2-2 exhibited a melting endotherm from the DSC scan of the sugar alcohol, mannitol. In this figure, the endotherm was obtained at a heating rate of 5°C/min. The $T_{m\ onset}$ is obtained by extrapolating the onset of the melting peak. $T_{m\ peak}$ is the maximum value of the peak. The enthalpy (ΔH) is determined by integrating the peak area. These three parameters characterize the endothermic melting event (Thomas, 2001).

Melting is considered to be a thermodynamic event - a fundamental characteristic of a compound, one that does not depend on instrumentation or heating rate. In the past, it was assumed that a compound's melting temperature would be the same, every time, regardless of how it was measured. Lee et al. (2011a) observed that Tm onset of the same material varied in different labs, and sometimes in the same labs. A change in Tm onset had been observed in the literature in various compounds, but especially in the sugar, sucrose. Heating rate dependence of the melting temperature had been reported and attempted to be explained in the literature by a number of researchers (Hurtta et al., 2004; Lappalainen et al., 2006; Räisänen et al., 2003). The work by Lee et al. (2011a) demonstrated that the three sugars tested (sucrose, fructose, and glucose) did not exhibit (true) thermodynamic melting, but instead started to decompose at the "melting temperature". Decomposition, evidenced by the detection of decomposition products by high pressure liquid chromatography (HPLC) analysis, resulted in the loss of crystalline structure of the crystals. Lee et al. (2011a) termed traditional melting as "thermodynamic melting" and this loss of crystallinity brought on by decomposition as "apparent melting". The researchers compiled Table 2-3 to compare the similarities and differences between thermodynamic melting and apparent melting.

To summarize Table 2-3, Lee et al. (2011a) reported similarities and differences between thermodynamic and apparent melting. Both types of melting result in the loss of crystalline structure and an endothermic peak. Thermodynamic melting is time independent, whereas apparent melting is time dependent. However, thermodynamic melting always occurs at the same temperature regardless of heating rate, while apparent melting temperature is heating rate dependent. Thermodynamic melting demonstrates constant enthalpy, and alternately, enthalpy varies in apparent melting with the changing heating rate. Enthalpy in a DSC peak in apparent melting materials is influenced by the loss of crystalline structure (or amorphization) enthalpy, as well as the enthalpy of the decomposition reaction. Thermodynamic melting materials do not exhibit a chemical change as they go through the phase

change from a solid to a liquid; however, in contrast, apparent melting compounds do exhibit a chemical change. The liquid material is no longer chemically identical to the corresponding solid, crystalline material. After apparent melting, the resulting sample measureable amounts of the decomposition products will be detectable, and upon cooling and reheating, the sample would exhibit a glass transition.

If apparent melting is associated with decomposition, then it is important to understand the decomposition of carbohydrate materials during heating. Raemy and Lambelet (1991) published a comprehensive review of heat behavior in carbohydrates, explaining that during heating there is first is a fusion event followed by exothermic decomposition. During the heating of carbohydrates there are other events that can also be observed including vaporization of water in hydrated carbohydrates, glass transitions, and crystallization of amorphous sugars.

In pharmaceutical and industrial research, compounds have also been observed to decompose below their melting temperature. Desilets et al. (2011) observed urea nitrate held at 100°C below its melting temperature (155 to 156°C) was completely degraded after 72 hours. The pharmaceutical industry uses "melt-degrade" terminology to identify compounds which immediately degrade after melting (Riga et al., 2007). In apparent melting, decomposition causes the collapse in crystalline structure, whereas "melt-degrade" terminology explains that the decomposition occurs immediately after loss in crystal structure.

In his review entitled "Thermal Behavior of Foods", Raemy (2003) described the main phenomena observed upon heating of carbohydrates as melting, release of crystallization water, decomposition, gelatinization of starch in the presence of water, and retrogradation of the gel, as well as glass transition, relaxation and crystallization of amorphous samples. These thermal events are best studied by thermal analysis and calorimetric techniques to further understanding of the thermal phenomenon. Providing a warning of which thermal process can present a hazard to industrial operations, the author observed that only decomposition, which he mentioned sometimes immediately follows melting, can be an issue. In our research we are not considering starch, so we will not discuss gelatinization or retrogradation. The melting, release of crystalline water and decomposition event will be considered individually below.

Melting in Carbohydrates

Before the work of Lee et al. (2011b), sugars with variable melting temperatures had been observed for many years. Early references (Fischer, 1908; Kofler and Sitte, 1950) describe the

decomposition of sugars occurring in the same temperature range as loss in crystal structure. Shafizadeh and Lai (1973) observed that reducing sugars seldom display a sharp melting point, and literature values often cover a wide range of melting temperatures. The variable melting temperature reported over the years has been explained in a variety of ways, including difference in measurement methods (Hurtta et al., 2004; Kofler and Sitte, 1950), origin of samples (Beckett et al., 2006; Hurtta et al., 2004), impurities present (Shah and Chakradeo, 1936); (Hirschmüller, 1963); (Kamoda, 1960); (Okuno et al., 2003); (Beckett et al., 2006), existence of polymorphs in the samples (Kishihara S et al., 2004); (Lee and Lin, 2007); (Lee and Da Chang, 2009), liquefaction of the samples (Tombari et al., 2007); (Trasi et al., 2011), thermal decomposition and/or mutarotation in addition to melting (Hurtta et al., 2004; Lappalainen et al., 2006; Lee and Lin, 2007; Sakamoto et al., 2006), and structural effects (Mathlouthi and Roge, 2012). These possible explanations are explained individually below.

Measurement Methods

Frequently, differences in measurement method are suggested as a reason for the variation observed in the melting temperature of sugars. Kofler and Sitte (1950) compared three methods for obtaining the melting point of sucrose and observed a variation of over 30°F (-1°C). They used the capillary method, a micro-heat table method, and the "heat-bench" method, which was a method they were developing to heat samples faster to avoid some of the problems of slower heating methods. They reported that other heating methods give different temperatures for the melting of sucrose and do not give consistent results. Hurtta et al. (2004) found the method for determining melting point of sucrose, glucose and fructose resulted in different melting temperatures. Metler Toledo FP 62 melting point apparatus and DSC at different rates were both used to measure melting temperature. The variation in observed melting temperature using the different methods is shown in Table 2-4. Looking at a particular sample, for example Sucrose A, onset temperature varied by 6°C between DSC and Metler Toledo FP 62 melting point apparatus.

Origin

Several researches noticed a difference in melting temperature depending on the source of the sugar sample. In Table 2-4, Hurtta et al. (2004) investigated bulk (industrial) (Sucrose A) and analytical grade sucrose (Sucrose B), fructose (A & B) and glucose (A & B) and found differences in melting temperature even using the same measuring technique between different sources of the material. Then

Hurtta et al. (2004) used DSC to determine melting temperature, and thermal decomposition was determined using thermogravimetric analysis (TGA). The bulk (commercial) sucrose had a lower melting temperature than the analytical grade as seen in Table 2-5. The enthalpy of the bulk sucrose (sucrose B) was found to be less than half the enthalpy of the analytical grade (sucrose A). Although both glucose samples were analytical grade, there were still differences observed between their melting behaviors. One had a higher onset, and the decomposition occurred at a higher temperature in glucose A compared to glucose B. The fructose was also analyzed from two sources. Bulk and analytical grade showed little difference in onset melting temperature and enthalpy, but showed a large difference in the shape of the peaks. The bulk fructose showed broad, wide peaks, and the analytical grade had narrower, sharper peaks.

Beckett et al. (2006) also studied sucrose from different commercial sources, as well as laboratory-recrystallized sucrose. Differences in the melting temperature and the enthalpy were found, depending on the source of the sucrose (Table 2-6). Products were recrystallized in a super-saturated solution of water and sugar. The mixture was heated to 128°C and removed from the heat, stirred (used to initiate crystallization) and allowed to cool to room temperature. The crystals were then dried overnight over P_2O_5. Endotherms were obtained by DSC scan from 25 to 200°C using a heating rate of 25°C/min. Two endothermic peaks (T1 and T2) were found in the Fisher Chemical (FC) and Tate & Lyle (T&L) samples that the researchers attributed to impurities. However, no invert sugar was detected, and when a small amount of invert was added (1% w/w), no significant change in the T1 isotherm was observed. Therefore, the peak was attributed to "another factor". Finally, potassium chloride was added to obtain a complete removal of the peak at 150°C, but in this case, the researchers ground the sample. The results comparing T2 showed a difference in melting temperature in the following order Silver Spoon (SP)>Lancaster (L)>Tate & Lyle (T&L)>Fisher Chemical (FC). They noted that the SP sugar was from sugar beets, whereas the T&L sugar was from sugar cane. As the researchers expected, the sugar from sugar beets (SP) had more impurities than the sugar from sugar cane (T&L); though, it was noted, processing and plants could affect the final mineral content of the sucrose.

Impurities Present

Beckett et al. (2006) investigated sucrose melting by DSC. An early, small endothermic peak at approximately 150°C was detected, which decreased when the sucrose was recrystallized with mineral salts. In contrast, absence of salts increased the appearance and size of this peak. Organic solvents and

polysaccharides had a minor effect on this peak compared to the salts. Unfortunately, these crystals were ground before DSC was run, which may have changed the results.

Existence of Polymorphs

Kishihara et al. (2001) suggested that different melting temperatures and melting behaviors are either because of different intermolecular bonds (hydrogen bonds) in the crystals or different conformations of the sugar crystals. The sucrose samples were observed by Kishihara et al. (2001) to exhibit two types of melting temperatures, a "low" (around 168°F) and a "high" (around 180°F). The higher melting temperature was suggested to utilize the "preferred" conformation, and lower melting temperature the less energetically stable form.

Lee and Lin (2007) investigated commercial and recrystallized sucrose and noted that the melting endotherms were not the same. Melting peaks were obtained by DSC at a heating rate of 10°C/min. The recrystallized sucrose showed two melting peaks (150 and 189°C), whereas the commercial sucrose showed only one peak (190°C). The recrystallized sucrose was obtained by recrystallizing from a methanol-analytic reagent grade sucrose solution at 60°C. The investigation utilized X-ray diffraction, which suggested the "presence of conformational polymorphs about the glyosidic linkage".

Lee and Da Chang (2009) compared sucrose crystallized from a furfuryl alcohol – water sucrose solution to commercial sucrose. Their results showed that sucrose crystallized in the lab exhibited a wide endothermic peak from 140 to 170°C, whereas commercial sucrose had one sharp melting peak around 185 to 189°C. The "inclusion of trace amounts of salts and water or degradation of sucrose did not offer a satisfying explanation" for the difference in melting peaks. Further work was done to identify what was causing the difference using x-ray diffraction, Fourier transform infrared spectroscopy (FTIR), and solid state nuclear magnetic resonance (SSMFR), which indicated "different degrees of conformational disorders" in the lab-crystallized sucrose. An interesting result occurred when sucrose was crystallized in a solution of sucrose at 25°C under a constant vacuum at different temperatures for different times. At 80°C for 12 hours, two large endothermic peaks were found, but at 80°C for 1 hour and at 140°C for 1 hour, the melting peak of the resultant crystal showed only one sharp endotherm at 189°C. The researchers proposed that this was caused by a polymorphic transformation that was possible at the higher temperature because of the decreased viscosity of the sugar solution.

Liquefaction of Samples

Tombari et al. (2007) proposed a theory of "spontaneous liquefaction" to explain the reported variation in melting temperatures. Sugars like fructose, glucose and galactose can isomerize to a tautomer that then cannot fit into the crystal structure, which would result in a lattice vacancy site. This vacancy creates a local region of "liquid" at a temperature below the melting point.

Similarly, in studying the dehydration of glucose, Trasi et al. (2011) hypothesized that when the sample is being dehydrated, it is also partially melting, and that cooling the samples results in partially molten regions. The cooled liquid regions then do not recrystallize, but form amorphous regions. Glucose was dehydrated at different temperatures in this study, and results showed the enthalpy of melting, onset melting temperature and peak melting temperature decreased when samples were dehydrated at higher temperatures. Again, it was attributed to melting and forming of amorphous regions on the surface of the crystal.

Thermal Decomposition/Mutarotation in Addition to Melting

A difference in onset temperature of melting (To), enthalpy (ΔH), and initial temperature of decomposition (Ti) was observed in sucrose, fructose and glucose (Hurtta et al., 2004). Tm onset temperature (To) as measured by DSC was compared to the initial decomposition temperature (Ti) as measured by TGA. The authors used these techniques to explore the relationship between melting and decomposition. TGA measurements were used to observe that at fast heating rates, melting occurred before thermal decomposition. Specifically, sucrose, at low rates of heating, decomposed before the melting temperature; but at higher rates, it decomposed after melting. "Anomalous melting temperature" was defined as the melting temperature of a compound where the compound is "in a different form" after going through melting. Hurtta et al. (2004) say that the anomalous melting temperature is strongly dependent on the rate of heating. Investigating the melting behavior of sucrose, fructose and glucose by DSC showed that the melting temperatures were heating-rate dependent. The conclusions drawn by the authors were that decomposition and mutarotation affected the melting temperature of glucose and fructose, and decomposition alone affected the melting temperature of sucrose.

Similar results were reported by Lappalainen et al. (2006) who studied xylose melting with standard DSC and stepwise DSC. The melting temperature (onset and peak temperature) increased as the heating rate increased. The heating of xylose was termed "anomalous" because it caused partial

thermal decomposition and mutarotation at the same time as melting. The Step Scan DSC allowed for separation of thermodynamic (reversible) and kinetic (non-reversible) components during analysis. This analysis showed a considerable kinetic component in the melting of xylose. The authors attributed the wide melting peak to decomposition, origin, quality, and maturation.

Sakamoto et al. (2006) published an abstract in the Proceedings of the Research Society of Japan Sugar Refineries' Technologists, which described the heat induced browning of two commercial sucrose samples, one that exhibited a relatively low melting point at 168°C, and one that had a relatively high melting point at 183°C. Holding the sucrose samples at 100°C for 48 hours produced heat induced browning, which could not necessarily be tied to impurities. The authors concluded that browning of the granulated sucrose after holding for 48 hours at 100°C was mainly caused by caramelization of residues of the reducing sugar, anhydro-sugars and/or melted sucrose derived from the breakdown or collapse of weaker regions of the crystal structure, rather than by impurities such as amino acid and polyphenols.

Structural Effects

Mathlouthi and Roge (2012) points out that the structural aspect of compounds is frequently neglected when trying to understand melting points of sugars. Mathlouthi asserts that the melting point of a crystal is governed by the hydrogen bonding ability of the molecules and the molecular packing in crystals (effects from molecular shape, size and symmetry) citing Katritzky et al. (2001).

There has long been an observance of different melting temperature by researchers. As discussed above, various explanations have been offered in the literature as to why these differences occur. None of these explanations seem to elucidate the entire set of data. Looking outside traditional food research, other explanations are presented.

Chemical Incompatibility/Chemical Interaction

Chemical interaction or chemical incompatibility is observed in pharmaceutical products. It is an interaction which leads to a loss in crystalline structure between excipients and the active ingredients in drugs. The loss of crystalline structure can decrease shelf life and may decrease the effectiveness of the active ingredients (Balestrieri F, 1996; Ceschel GC, 2003; Kiss D et al., 2006; Oliveira GGG, 2005).

Practically, chemical interaction between the excipient and the active ingredient will produce a new melting peak in the DSC. The new melting temperature is usually located between the two melting temperatures of the individual ingredients.

Figure 2-4 shows the effect of chemical interaction using aspirin and magnesium stearate. In this DSC scan, it can be observed that aspirin by itself demonstrates a sharp melting peak on the right hand side of the thermogram while magnesium stearate exhibits a wide melting peak on the left. A blending of the two materials presents one endotherm at a Tm onset between the Tm onsets observed from the individual components. The lowering of the melting temperature has been ascribed to the contact between the drug and excipient, where the excipient forms a surface film on the active ingredient particles that may promote the decrease in the active ingredient's melting temperature (Miller and York, 1988).

Many researchers attempt to recrystallize sucrose, to either test the effects of added impurities on the melting temperature or to purify the sucrose (to test the removal of impurities). Okuno et al. (2002) introduced various cations (Na^{+}, K^{+}, Ca^{++}, Mg^{++}), anions ($HCO3^{-}$ and Cl^{-}) and organic acids, and found them all to affect the melting point of the sucrose. When monovalent cations (Na +, K +) were present in the sucrose solution before crystallization, an increased melting point for the sucrose crystal was observed. In contrast, when divalent cations (Ca 2, Mg 2) were present in the sucrose solution, a decrease in the melting point of the sucrose crystal was observed. When hydrogen carbonate ions (HCO^{3-}) were present in the sucrose solution, sucrose crystals with high melting point were produced. Chloride ions appeared to have no effect.

Further work by Okuno et al. (2003) recrystallized sucrose in the presence of Potassium chloride (KCl), which changed its DSC melting characteristics. Initial samples and KCl recrystallized samples all exhibited three peaks during melting. However, Figure 2-3 displays an increase in “peak purity” with increasing KCl content. An increase in “peak purity” is described by Okuno et al. (2003) as an increase in height and a decrease in the number of other peaks (moving to one narrow peak). Sucrose was also recrystallized in a raw sugar solution, and when this recrystallized sugar was analyzed it exhibited a single sharp peak (similar to the high KCl recrystallized sucrose).

Commercial sucrose investigated by Okuno et al. (2003) varied in melting temperature from 170 to 192°C. The researchers attributed the differences in melting temperatures to impurities. For comparison purposes, the sucrose was analyzed for impurities by measuring the reducing sugar content and the conductivity (ash). The melting point was reported to have a tendency to increase with small

quantities of impurities in the sugar. Typically, the melting temperature decreases with increasing impurities. The results from the KCl studies and the analytical analysis of the commercial sucrose tested were different than that reported by Hirschmüller (1953) and Kamoda (1960.) The literature values showed a decrease in melting point with an increase in impurities, whereas the KCl research reports an increase in melting temperature with an increase in impurities: inorganic salts in the case Kamoda (1960) and degradation products in the case of Hirschmüller (1963). Okuno et al. (2003) stated that the difference in melting point is attributed to a difference in crystal structure (because of the impurities), but no data was given to demonstrate a difference in crystal structure.

Chemical incompatibility can be observed with a variety of excipients. Lactose was evaluated for compatibility with two active ingredients, etamsylate and fluconazole (Desai et al., 2003). Each of the samples (lactose, etamsylate, and fluconazole) and mixtures of these materials were compared in DSC at a heating rate of 10°C/min. In this work, mixtures of lactose with etamsylate showed different peaks in the DSC than results found by evaluating each of these materials alone, as seen in Table 2-7. Etamsylate has a peak at 136.7°C and lactose at 145.0°C. When the samples are combined, there are two peaks; however the etamsylate peak shifts slightly at 131.4°C, and a new peak is observed at 118.5°C. X-ray diffraction confirmed that the peaks present in pure etamsylate are absent in the mixture (of lactose and etamsylate), which confirms a loss in crystalline structure from the active ingredient. This same effect was seen with mixtures of fluconazole and lactose. A similar observation was found when evaluating lactose and other drugs, such as acetylcysteine, indomethacin, and glimepiride (Cides et al., 2006; Kerc et al., 1992; Venkataram et al., 1995).

Glass Transition and Melting

Several studies investigated the impact of heating rate during melting on the glass transition of sugars (Jiang et al., 2008; Vanhal and Blond, 1999). Vanhal and Blond (1999) investigated the effects of heating rate, holding time and temperature on the Tg of sucrose held at its melting temperature (190°C). The Tg values for amorphous sucrose decreased in the final heating temperature range of 190 to 210^{o}C and then increased in the final heating temperature range of 215 to 225^{o}C. The decrease in Tg in the sucrose samples was attributed to the formation of small molecular weight components via bond breaking (under low heat conditions). The increase in Tg values was due to formation of various high molecular weight components via polymerization (under high heat conditions). Jiang et al. (2008) also found a similar trend of dependence of heating rate on the Tg, which was also attributed to the

caramelization, though Jiang et al. (2008) found different effects on the Tg depending on the stage of caramelization. Stage 1 is the occurrence of small molecules in the caramelized mixture that decreased the Tg. Stage 2 is the polymerization of materials that lead to larger molecular weights, leading to an increase in Tg.

Roos (1993) investigated the melting temperatures and fusion temperatures (Tf) of 18 sugars and sugar alcohols. Results are given in Table 2-8. Melting temperatures were determined in the DSC at a heating rate of 5°C/min. When comparing the Tf to the Tg in a ratio Tf/Tg, Roos found most sugars had a ratio of 1.35 ± 0.02, which was similar to results reported by Slade and Levine (1991). The values for this ratio were higher for arabinose, xylose, galactose, sorbose, and xylitol. Polymers with high Tf/Tg ratios are considered to be easy to crystallize. The melting temperatures Roos reported are in general higher than the values reported by Raemy and Schweizer (1983), but lower than values reported by Slade and Levine (1991).

Slade and Levine (1991) published a detailed review of water activity and relations in food including many physical properties of materials. A large table was presented analyzing glass transition, Tg', Wg' and melting temperatures for over 100 sugars and sugar alcohols. Interestingly, the results reported by Slade and Levine (1991) did not show a range of melting temperatures for any of the sugars, nor was it reported that melting temperatures were hard to obtain or that there were any problems with repeatability.

Table 2-8 expands on the table demonstrating large variation in reported melting temperatures of sugars and related compounds from Roos (1993). A large variation in reported melting temperatures of sugars and related compounds was revealed. If a compound is a thermodynamic melting material, the melting temperature should occur within a relatively tight range each time it is measured. For example, Lee et al. (2011a) reported indium to have a Tm onset variation of <1°C and mannitol <0.5°C in the heat rate range of 1 to 25°C/min. A large variation in the reported melting temperature would tend to indicate an apparent melting material, since apparent melting (a kinetic event) would be heat rate dependent. Thermodynamic melting would be independent of the heating rate.

Lee et al. (2011c) investigated the effect of heating conditions on the glass transition of sucrose. Amorphous sucrose samples were prepared by heating at three different scan rates (1, 10, and 25°C/min) using a standard differential scanning calorimetry (SDSC) method and by holding at three different isothermal temperatures (120, 132, and 138°C) using a quasi-isothermal modulated DSC method. This research showed that, depending on the heating conditions employed, a different amount

and variety of sucrose thermal decomposition components may be formed, giving rise to wide variation in the amorphous sucrose Tg values. Procedures that used lower temperatures for longer times to produce amorphous sucrose exhibited lower Tg values, larger ΔCp values, and broader glass transition ranges.

A majority of the work on heating rate dependence of the melting temperature was done on commonly used sugars (fructose, glucose and sucrose). Examining literature studying related carbohydrate materials will give an insight into its thermal behavior.

Sugar Alcohols

Barone et al. (1990) studied sublimation, vaporization and fusion of nine polyhydric alcohols including erythritol, adonitol, D-arabinitol, xylitol, dulcitol, D-mannitol, D-sorbitol and myo-isositol. The enthalpy and temperature of fusion (melting) was measured using the DSC with a heating rate of 1 K/min. The temperatures reported at the onset of fusion and the results are shown in Table 2-9. Good agreement was obtained between Barone et al. (1990) and those reported in the literature. D-sorbitol had a fusion temperature similar to the B form reported by Quinquenet et al. (1988), but the slight difference was assumed to be contamination by the A form. Sorbitol can be difficult to characterize because it can crystallize into different crystalline forms. Quinquenet et al. (1988) characterized the three crystal forms (A, B, and Γ forms). The different crystalline forms have different melting temperatures. The crystals can rotate between forms as the crystal ages.

Gombas et al. (2003) studied the melting of sorbitol, mannitol and mixtures of the two. Sorbitol was melted in the DSC after which it was cooled and vitrified to an amorphous state. β-D-mannitol melted on the first heating at 165°C and was shown after cooling to change to α-D-mannitol on the second melting. Sorbitol showed a melting temperature of 96.8°C. Combinations of sorbitol and mannitol showed two melting peaks (not the single melting peak seen in some pharmaceutical compounds described as chemical interaction in the section above). Combinations were made at 0% sorbitol and 100% mannitol, 10%, 30%, 50%, 70%, 90%, 100% sorbitol. A heating rate of 3.5K/min from 25 to 200°C was initially applied; samples were then cooled in liquid nitrogen and reheated from -20 to 200°C at the same rate (3.5 K/min). In the mixtures, a decrease in mannitol's melting temperature was observed, because mannitol dissolves in sorbitol melt. The melting temperature of sorbitol was only slightly affected by the presence of mannitol.

Bruni et al. (2009) found no difference in the melting temperatures between α and β mannitol. Samples were melted in the DSC from 25 to 200°C at a rate 2K/min. Melting the β and δ mannitol was found to always result in the α form. TGA was used to verify the melting events (room temperature to 180°C at 10°C/min) and X-ray patterns to verify the crystal form.

Lee (2010) tested both mannitol and sorbitol as possible standards more like the materials tested (sucrose, glucose and fructose) than indium. Sorbitol was found to have too much variation to be used in the study by Lee (2010). Mannitol was found to have a melting temperature that was very reproducible, and so it was used as a characteristic material.

Dehydration Studies

Raemy (2003) discussed release of crystallization water as a main phenomenon in the heating of hydrate carbohydrates. In raffinose pentahydrate, dehydration has been shown to cause a loss in crystalline structure (Bates et al., 2007). It is important to investigate dehydration and determine its effect on crystalline structure and observed melting temperatures.

Bates et al. (2007) dehydrated raffinose pentahydrate in glass scintillation vials in a 60°C vacuum oven and noticed a drastic decrease in crystallinity after two hours of dehydration. Water loss was verified by Karl Fisher, and the crystallinity was analyzed by X-ray diffraction. The loss of crystallinity was attributed to defects in the crystals, providing a driving force for conversion to the amorphous state. The dehydration was done below the melting temperature at 60°C. The loss of crystalline structure was attributed to loss of water and collapse of the crystalline region. Bates et al. (2007) explained that as water leaves the crystal lattice during dehydration, vacancies are formed. These vacancies are crystal defects, which lead to disorder and ultimately collapse of the crystal structure resulting in amorphous crystals.

Cheng and Lin (2006) also studied the dehydration and rehydration of raffinose pentahydrate using DSC, TGA and FTIR. Raffinose was dehydrated using DSC and TGA. The TGA showed a loss in weight in several stages. In order to understand the correlation between the loss in weight and corresponding DSC peak, samples were preheated to 62, 81 or 125°C. If raffinose was preheated to 81°C (and lost three molecules of water), its rehydration process was very difficult; it would not regain its water molecules of hydration when held isothermally at 70% RH at 30°C. Results of this study provide evidence that raffinose pentahydrate dehydrates in a stepwise manner, losing one molecule of water at a time.

Trehalose dihydrate was studied by Ding et al. (1996). Dehydration of the trehalose was performed at 95°C (at ambient pressure) and 70°C (at vacuum conditions), which was below the literature reported melting temperature (188°C) and found the heat required for dehydration resulted in the loss of crystalline structure of the sugar. The author hypothesized that hydrated sugars lose water and therefore the crystalline structure, although this was not observed by Ding et al. (1996). Willart et al. (2002) found that the rate of dehydration affected the crystalline structure. A fast rate resulted in amorphous trehalose, whereas a slower rate resulted in a polymeric crystalline structure.

Shafizadeh and Lai (1973) found using DTA, that water of hydration of trehalose was lost around 100°C, whereas the anhydrous crystals melted at a higher temperature (215°C). The thermogram is shown in Figure 2-5. This loss in water can be seen in Figure 2-5 by observing the peaks in DTA that occur at the same time as a weight loss in TGA. The melting of the anhydrous crystals is seen by the endothermic peak at 215°C, which does not have a corresponding loss in weight.

Several studies considered trehalose dihydrate because of its importance as an excipient (Landin et al., 2005; Taylor and York, 1998). Taylor and York (1998) observed the dehydration of trehalose dihydrate using hot-stage microscopy, crystallography and thermal analysis by TGA and DSC. It was found that trehalose dihydrate can be crystallized to the anhydrate by heating. Two routes of crystallization were found that are primarily dependent on the particle size of the crystals. A difference was found between large and small particle size; the large particle size going directly to anhydrate via a solid-solid transition, while small particles crystallize from an amorphous liquefied phase. A temperature range of 25 to 230°C in the DSC was used with rates from 1 to 10°C/min. In the TGA, a similar temperature range was used with rates from 0.1 to 10°C/min. They observed that dehydration was affected by heating rate, with complete dehydration being accomplished at lower temperatures when the heating rate was very slow. They tested two particle sizes of trehalose dihydrate. As seen in Figure 2-6, results from the DSC show that slower heating rates decrease the appearance of the endotherm at 110 to 120°C. There is also a decrease in enthalpic magnitude of the peak at 101°C. They attribute these changes to a loss in sensitivity by the DSC. They also note the appearance of the large exotherm at approximately 170°C which was attributed to the crystallization of the anhydrate crystal.

Thermal Decomposition

After considering melting and release of the crystalline water, Raemy (2003) next discussed decomposition as the main phenomenon in the heating of carbohydrates. Raemey warned that

decomposition presented the most trouble in food processing. Decomposition of carbohydrates is a complicated process with many intermediates and pathways. Figure 2-7 illustrates the high level schematic of the early stages of decomposition of a hexose. From this level, it seems very simple, but in actuality there can be hundreds of compounds formed. The decomposition of hexoses involves a triple dehydration to the compound 5-hydroxymethylfurfural (HMF). The review by Lewkowski (2001) suggests two separate pathways from a hexose to HMF: a route that contains linear intermediates and a route with cyclic intermediates. Figure 2-8 illustrates a high level schematic of the two pathways with only the most representative products. Van Dam et al. (1986) and Cottier et al. (1989) showed that the decomposition of sugar can lead to approximately 37 different products, so a complete pathway can be very complicated because of the various intermediates. Further decomposition of HMF leads to levulinic acid and formic acid. After HMF is formed, polymerization that leads to humic acids can also occur. Furfural is formed by the triple dehydration of pentoses or from the loss of carbon from HMF (Fagerson, 1969). The decomposition pathway can also result in the formation of oligosaccharides (Golon and Kuhnert, 2013; Heyns et al., 1966).

Ramos-Sanchez et al. (1988) explains a three-step decomposition of sugars, first a loss in water/fusion, then what they term as early decomposition, then a slightly endothermic inflection which occurs just before combustion. Ramos-Sanchez et al. (1988) studied 24 sugars using dynamic thermal analysis (DTA) and dynamic thermal gravimetric (DTG) over temperatures ranging from 25 to 700°F. The sugars studied were: D-ribose, D-xylose, D-arabinose, L-arabinose, D-mannose, D-glucose, D-galactose, L-rhamnose monohydrate, D-fructose, L-sorbose, D-trehalose dihydrate, D-maltose monohydrate, sucrose, D-lactose monohydrate, D-melibiose monohydrate, D-cellobiose, D-raffinose pentahydrate, D-melezitose dihydrate. Also studied were inulin, dextrin, starch solution, cellulose, Ficoll (a synthetic polymer of sucrose), and hyaluronic acid, which are typically classified as complex carbohydrates. Thermal stability of disaccharides was found to be in the following order, from most to least stable: cellobiose> trehalose> lactose and maltose> melibiose> sucrose. For monosaccharides, the ranking was glucose > galactose> fructose. The following conclusions were reported:

(a) Aldoses are more stable than ketoses.

(b) The β-glycosidic linkages confer more thermal stability than α-glycosidic linkages.

(c) The β 1-4 linkages are more stable than α 1-6, the α 1-1 and α 1-4 being in between.

Rey et al. (1988) conducted similar studies on sugar derivatives, including amino sugars, sugar alcohols, nucleosides and nucleotides. It was reported that there was an excellent agreement between

results observed for regular sugars versus these related products. In both cases, the stability of the ribofuranosyl ring was found to be greater than the pyranosyl rings. Polyols were reported to be more stable than sugar analogs and much more stable than sugar acids. The hydrogenation of sugars slowed the onset of decomposition by 30°C.

A survey of the thermal breakdown of sugars (arabinose, xylose, mannose) and sugar alcohol (arabinitol) showed that sugars of similar carbon number had similar degradation products (Räisänen et al., 2003). Table 2-10 tabulates the main Gas Chromatography (GC) chromatogram peak after pyrolysis of the different sugars in this study. Samples were pyrolyzed at 500°C and 550°C in a pyrolyzer, which was attached to a GC. In Räisänen's study (Räisänen et al., 2003) when comparing the values of Ti (degradation starting) with the melting values of To (onset) and Tp (peak) "it was obvious in the case of sugars, degradation begins before melting". Pentoses in this study (arabinose and xylose) had different decomposition products from the hexose (mannose) and the sugar alcohol (arabinitol). In pentoses, the major decomposition product was found to be 2-furancarboxaldehyde, and in hexose it was found to be (2H)-furan-3-one. Main pyrolysis products were found to be in seven classes of compounds: (i) furanes, (ii) pyranes, (iii) cyclopentanes, (iv) cyclohexanes, (v) anhydroglucopyranoses, (vi) dianhydroglucopyranoses, and (vii) saturated fatty acids.

Maga (1989) published a review that described the thermal decomposition of different carbohydrates. The decomposition can be very complex; the pyrolysis of glucose, for instance, resulted in over 130 different compounds (Heyns et al., 1966). Maga (1989) reported that the literature indicates temperature, amount of moisture, time and pH affects types and amounts of observed degradation products. In regards to sucrose, Maga (1989) reports that a melt state of sucrose degraded into glucose, fructose and trisaccharides quite rapidly. Lactose was also studied extensively because of the heat treatment of many dairy products. Many lactose decomposition products were reported, including disaccharides, andyro sugars and lactulose. Cellulose thermal breakdown goes through the intermediate levoglucosan (Glassner and Pierce, 1965).

Shafizadeh and Lai (1973) researched the thermal transformation and rearrangements of β-cellibiose and trehalose using dynamic thermal analysis and various methods to study the formed compounds. Cellibiose and trehalose were heated at a rate of 15°C/min. The cellibiose (a reducing sugar) was reported to show "concurrent melting and thermal anomerization, followed by condensation and ultimate decomposition" whereas the non-reducing sugar (trehalose) showed dehydration, melting, polymerization and decomposition. The DTA indicated that water was lost around 100°C, and then the

anhydrous crystals melted at 215°C. Shafizadeh and Lai (1973) divided the thermal decomposition of oligosaccharides into three types of thermal transformations: "At low temperatures dehydration and melting primarily occur. At temperatures above the melting point, free sugars are produced that can anomerize and participate in inter- and intra-molecular condensations; glucoside and anhydro sugar intermediates can also be generated, which yield inter- and intra-molecular transglucosylation products. The consequence of higher temperatures is the thermal decomposition of the sugar moiety".

Richards (1986) claimed that crystalline sucrose was stable for several hours at 150°C, but if a melt state of the sucrose was created, it degraded into glucose, fructose and trisaccharides quickly. The melt state held at 150°C, and degradation compounds were determined by HPLC. Crystalline sucrose was not tested in these experiments. Adding either glucose or sodium chloride enhanced the degradation. He found that the first degradation step in sucrose decomposition was sensitive to catalysis by protonation of the glyosidic oxygen.

Several studies have been carried out on the decomposition of D-xylose (Lappalainen et al., 2006; Shafizadeh, 1971; Shafizadeh et al., 1971; Tanaka and Nakamura, 1983). Shafizadeh et al. (1971) obtained a melting temperature of 155°C at a heating rate of 15°C/min. The melting endotherm peak was found to be rather wide and unsymmetrical, which was attributed to impurities, though the authors did not test or report any impurities to support this conclusion. The wide endotherm could also be due to the presence of both the α and β forms of the xylose. For this reason, a series of temperatures was tested, and a ratio of the two polymorphs at the various temperatures was reported as shown in Table 2-11. Decomposition was carried out at 250°C in the TGA and analyzed by TLC (thin layer chromatography) and GLC (gas/liquid chromatography) which showed a cleavage of the glycosidic group, polymerization of the glycosyl moiety, and decomposition within a narrow range. $ZnCl_2$ was added as a "catalyst"; cleavage and polymerization reactions occurred at a lower temperature then in the xylose without added $ZnCl_2$.

The work of Tanaka and Nakamura (1983) was primarily done to determine the kinetics of decomposition for D-xylose. Three methods obtaining kinetic data were compared (gas chromatographic method, Ozawa's method, and Friedman's method). The gas chromatographic method was a new method used in this study, which heated the sugars to different temperatures, and each temperature showed the order of reaction becomes gradually larger (1.4 at 160°C and 1.8 at 200°C) as shown in Table 2-12. Order of reaction, rate constant and Ln A (activation energy) were calculated from the relation between the residual weight of water and time at each temperature. Order

of reaction was also calculated using the Friedman's method to be 1.73. Activation energies also showed good agreement between methods.

Lappalainen et al. (2006) tested the decomposition of xylose and concluded that the difference in melting temperatures with different heating rates was because of thermal decomposition. Table 2-13 presents the T_m onset (melting onset), T_m peak (melting peak) and ΔH (enthalpy) from DSC and T_f (decomposition temperature) as measured by TGA. It can be seen in the table that in some cases the T_f was actually below the $T_{m\ onset}$. Two samples, marked non-dried, were measured as-is. The rest of the samples were dried over phosphorus pentoxide.

The first step in the thermal decomposition of citric acid is also a dehydration step, changing citric acid into aconitic acid (Barton and Ollis, 1979). The work by Barbooti and Al-Sammerrai (1986) found that citric acid decomposes slowly above 148°C and increases in rate after the material melts at 153°C. The decomposition was found to follow the Jander diffusion mechanism, being a first order reaction.

The relationship between decomposition, melting, and other thermal events has been investigated and reported on thoroughly in the literature over time. Various explanations have been given as to how the different events influence one another. Lee et al. (2011a) gave the most recent input showing that in certain sugars, decomposition occurs that produces a loss in crystalline structure of these sugars, namely sucrose, fructose and glucose. Various techniques can be used to investigate these events, which can give different types of information to evaluate the processes involved in heating various sugars and other carbohydrates.

Thermal Analytical Techniques

Calorimetry, Differential Thermal Analysis (DTA) and DSC are commonly used to give reproducible data, which can be used to characterize food (Raemy and Lambelet, 1991). Understanding these techniques, how the data is gathered and what kinds of data they produce will help with understanding which techniques can be used for further research. A detailed discussion will be provided on several DSC techniques and thermal gravimetric analysis (TG or TGA).

Standard Differential Scanning Calorimetry (SDSC)

SDSC, which is generally abbreviated as DSC, is a thermal analytical technique where the difference in the amount of heat absorbed or given off is measured between a substance and a

reference material. The difference is measured as a function of temperature, while the substance and a reference material are subjected to a controlled temperature program (Note: This definition is the one that's approved by the International Confederation for Thermal Analysis, August 1977). There are two types of DSC instruments; power compensation and heat-flux DSC.

Figure 2-9 presents a schematic diagram of the power compensation DSC. In power compensation DSC, the reference and the sample pans each have a separate heat source (or furnace in the diagram). In this case, the sample and reference (usually an empty pan) undergo the same heating profile. The difference in energy needed to be put into the sample is measured and compared to the energy needed to be put into the reference. If the sample is undergoing a thermal event, then it may need more or less energy than the reference. The heat output of the two furnaces at any given temperature is measured and directly appears as the total heat flow signal plotted as a function of temperature, or time, which is a DSC thermogram.

Figure 2-10 is a schematic of a heat-flux DSC. In heat-flux DSC, the sample and reference are in the same heating chamber. Each pan is placed on a separate raised platform, which is attached to a sensor. The sensor is composed of a copper-nickel alloy named constantan. A thin wall tube lines the edge, which creates thermal resistance. The raised platforms are covered with a thin chromel disk and function as a thermocouple to reduce the sensitivity of the sensor to the pans. A chromel wire is attached to each chromel disk (Danley, 2003; Lee, 2010). In typical heat flux DSC instruments, heat is transferred from the furnace through the constantan body and up through the sample and reference pans. The temperature difference between the sample and reference thermocouple is measured and sent as an output directly as heat flow that is displayed as a thermogram.

Further advances occurred in heat-flux DSC in the Q2000 DSC Instrument from TA Instruments, which utilizes a Tzero thermocouple (a chromel/constantan wire). This wire is located equidistant from the sample and reference sensor platforms and measures and controls the furnace and temperature. The Tzero thermocouple helps improve baseline stability and resolution in the instrument, which helps with heat capacity measurements and quantifying and identifying weak and broad transitions (which might otherwise be missed).

A heat-flux DSC has a better baseline than a power compensation DSC. In heat-flux DSC there is a smaller temperature difference between the furnace and the sensor (since the pans are both in the same cell).

Heat flux DSC (as well as power compensation DSC) requires calibration. In the Q2000 DSC, the Tzero thermocouple must also be calibrated. This is done using a two-step process. First, the calibration is run with no pans in the cell, and the instrument measures the difference in the two platforms. Secondly, a known sample is run. Usually indium is used (melting temperature of 156.6^{o}C, ΔH of 28.71 J/g). Temperature and enthalpy calibrations are performed by heating indium through its melting transition at a heating rate of 10^{o}C/min.

The difficulty with standard DSC is that it only measures heat flux, and it is difficult to say if the difference in temperature fluctuation is because of a thermodynamic or a kinetic event. It becomes more complicated to interpret the results if events overlap. In this case, another type of DSC, modulated differential scanning calorimetry (MDSC), is needed. MDSC measures both the total heat flow and its heat capacity component. From this data the kinetic component can be obtained from their difference. This is done by using two heating rates simultaneously.

Modulated Differential Scanning Calorimetry (MDSC)

MDSC was developed to overcome the disadvantages of SDCS by applying two simultaneous heating rates to the sample: a linear or average heating rate (same as in SDSC) and a modulated or sinusoidal heating rate. Thomas (2006) has written a complete manual entitled "Modulated DSC Technology," that explains the use and practice of MDSC. Figure 2-11 tracks the heating used in MDSC. The blue line displays the average temperature and the line above and below shows the modulated temperature around the average. The red line exhibits the average heating rate, which the modulated heating rate is plotted against. From this plot, it is obvious that although the average heating rate does not change, at any given time it is different depending on where in the modulation it is. Typically, the average temperature is always increasing throughout the test. Table 2-14 shows what signals can be obtained from the MDSC. Figure 2-12 charts these signals plotted in a thermogram. Total heat flow is the only measured signal, and the rest are calculated based on equations in Table 2-14. The table demonstrates that there is much more information available from the MDSC. In heat-flux DSC, only the total heat flow is available, whereas in MDSC the total heat flow can be separated into the reversing and non-reversing heat flow. The reversing heat flow is generally caused by heat capacity and changes in heat capacity caused by glass transitions and loss in crystalline structure. This fraction is called the heat capacity component (also termed the reversing heat flow) and is shown as the reversing heat flow signal in a MDSC thermogram. The non-reversing heat flow does not respond to changing heat rate, and can

be calculated by subtracting the reversing heat flow from the total heat flow. This fraction is caused by kinetic processes, such as decomposition, evaporation, chemical reactions, and crystallization. This fraction is called the kinetic component (also termed the non-reversing heat flow) and is shown as the non-reversing heat flow signal in a MDSC thermogram. The separate signals of the MDSC are calculated based on the equations shown in Table 2-14. Calculation of signals required the ability to control the heating rates applied to the sample. During melting, there is equilibrium between the crystalline and amorphous phases, and the sample's temperature remains invariant until the sample has melted. Therefore, regular MDSC should not be used to separate the total heat flow into components during the loss of crystal structure.

"Quasi-isothermal" MDSC

A variation of MDSC has been developed which is used to measure heat capacity and changes in heat capacity during thermal and kinetic events. This method, called quasi-isothermal MSDC, involves a small temperature modulation, which is applied to a constant average temperature for a relatively long period of time. Changes in heat capacity will indicate a change in structure caused by a thermal event. A kinetic event or process can be observed using this method by measuring a change in heat capacity (C_p). Table 2-15 shows the signals used in quasi-isothermal DSC. In this method, a change in C_p is seen in the reversing C_p signal because the reversing C_p is associated with the modulated heating rate. In the case of quasi-isothermal DSC, the average heating rate is zero.

Lee (2010) demonstrated the use of two types of quasi-isothermal MDSC methods to investigate the loss of crystalline structure in glucose, fructose and sucrose. In the first type, which was termed quasi-isothermal MSDC, the modulated heating rate was applied at a single temperature (below the melting temperature), until the crystalline structure was removed. In the second type, which was termed stepwise MDSC, the modulated heating rate was applied to the sugar for fixed time increments (e.g. 30 min) at increasing temperature steps (e.g. 60 to 120°C) across the range of temperatures over which the loss of crystalline structure occurred.

Thermogravimetric Analysis (TGA)

TGA is a thermal technique that involves heating at a controlled rate, as in the DSC, but it also measures the amount and rate of weight change in a material. The analysis is performed in an open pan to allow weight loss and can be used to understand the thermal or oxidative stability of a material. The idea is that if a material breaks down, or oxidizes, the resultant compounds will have smaller molecular weights and will volatilize from the sample, causing a loss in weight. TGA can measure weight loss or gain of a material caused by many different processes like decomposition, evaporation, gas adsorption or desorption.

TGA can be important for monitoring the decomposition of sugars (Hurtta et al., 2004; Lee et al., 2011a). As the heating rate is applied, the sample increases in temperature. When the sugar reaches a point in decomposition where a corresponding loss in weight happens, it is recorded by the balance. Correlating the temperatures, times, events and loss in weight can give insight into the types and kinds of events occurring in the samples. Thermodynamic melting would show a thermal event with no loss in weight, whereas decomposition would show both a loss in weight and a thermal event.

In TGA, the sample is suspended inside a furnace, which is flushed with a type of purge gas. Different purge gases are used including air, nitrogen, oxygen and helium. A conductive gas such as helium is often used to improve contact between the sample and the thermometer, since the heat does not touch the sample directly in TGA. When running the TGA, it is important to establish a stable baseline. This can be done by controlling the rates of gas flow. High rates of gas flow can cause an undesirable baseline by causing movement (or buoyancy effects) in the pan balance. This can cause a loss in weight when one does not exist, or mask a small loss in weight.

Weight change in the TGA is measured by photo detectors in the balance. With zero weight change, there is equal light in each of the two photo detectors. The sample is then heated by the furnace at a predetermined rate and temperature. If a kinetic process occurs, which involves a loss or gain in weight by the compound, the light will be disrupted (and it will not be equal in the two photodectors). Current will then be generated to cause the balance to equilibrate to equalize the light. This adjustment to achieve equilibration sends a signal regarding the weight change, which is recorded and displayed along with information about the temperature of the sample and the elapsed time.

The cause of the loss of crystalline structure in sugars can be explored by comparing the temperature at which the TGA weight starts to decrease (thermal decomposition) to the temperature, which has been shown to be the beginning of the loss of crystalline structure (onset of melting) in the

DSC. A thermogram from the TGA can provide several characteristics including the weight loss and derivative weight loss (%/C) as seen in Figure 2-13. Plotting derivative weight loss against temperature will show the temperature, which has the greatest loss (indicating decomposition temperature). A derivative temperature plot (°C/min) can monitor the heating rate of a material during a phase transition, such as the loss of crystalline structure. During a phase change, increased temperature would be needed for the phase transition (latent heat) and would not be available to raise the temperature of the sugar. When the compound is not undergoing a phase transition, heat would be applied as sensible heat, resulting in a temperature increase. Therefore, monitoring the heating rate will tell if a sample is using latent heat or sensible heat and will determine whether the onset of the phase transition can correspond to the onset of melting.

Sugars, the small, relatively simple molecule, are one of the most powerful building blocks in nature. Sugars have been investigated because their significance in nature and in the food industry. Special focus has been given to the thermal events that occur in sugars as described by Raemy (2003); particularly melting, loss of crystalline moisture and decomposition. An in-depth look at melting has been discussed including the definition of thermodynamic and apparent melting from Lee et al. (2011a). A focus on the various explanations for reported temperature dependence on Tm onset has been laid out. Thermal decomposition, including major products from carbohydrate decomposition, has been reported. Various methods to investigate thermal processes have also been investigated. This overview has prepared a foundation for a further investigation of various carbohydrate compounds to further apply the work of Lee et al. (2011b) and Lee et al. (2011a) to materials beyond sucrose.

Figures and Tables Chapter 2

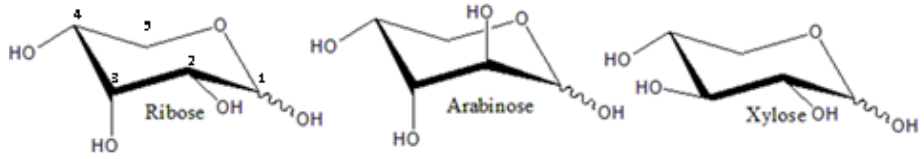


Figure 2-1: Structure of various Monosaccharides

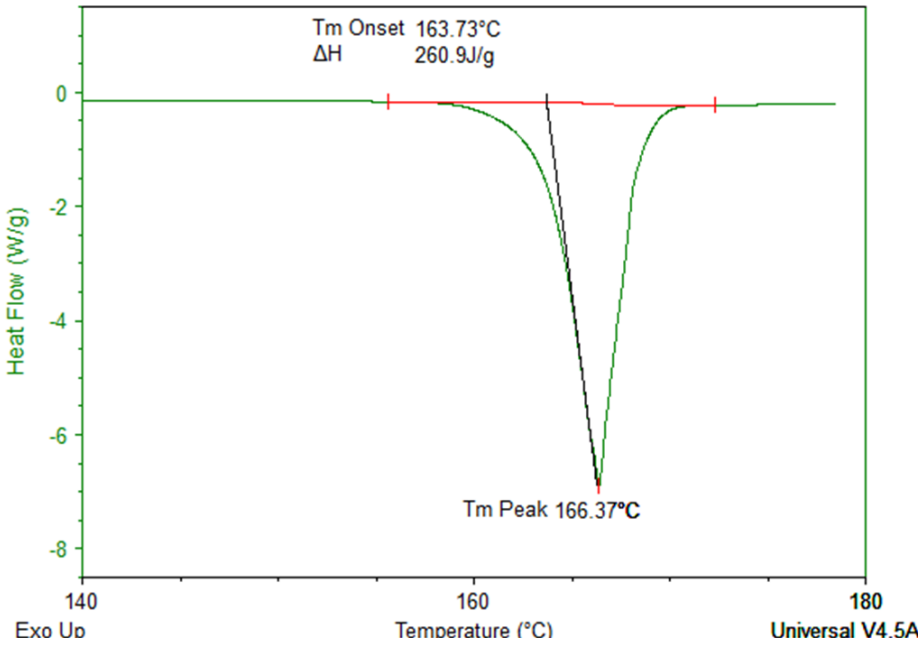


Figure 2-2: DSC melting endotherm of mannitol at 5°C/min

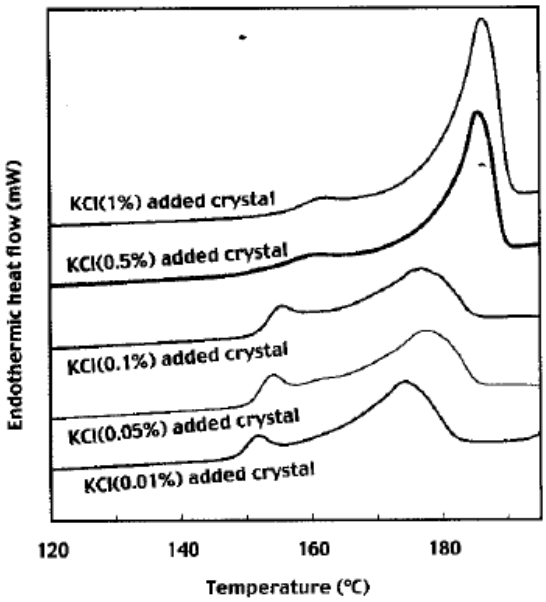


Figure 2-3: DSC endotherms of sucrose crystallized with increasing amounts of KCl (Okuno et al., 2003)

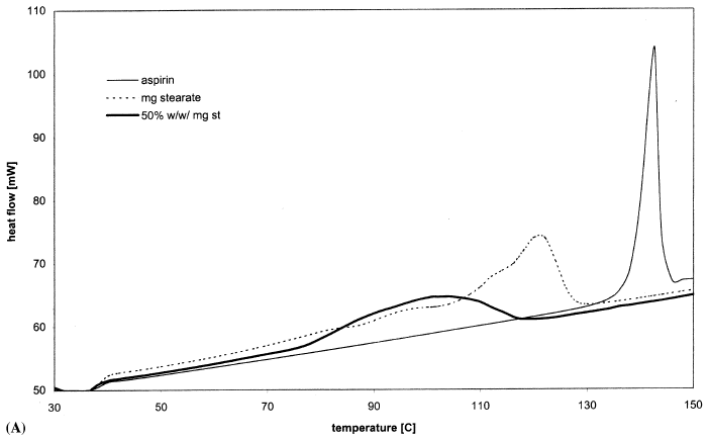


Figure 2-4: SDSC thermograms for aspirin, magnesium stearate and a 50/50 mixture (Wissing et al., 2000)

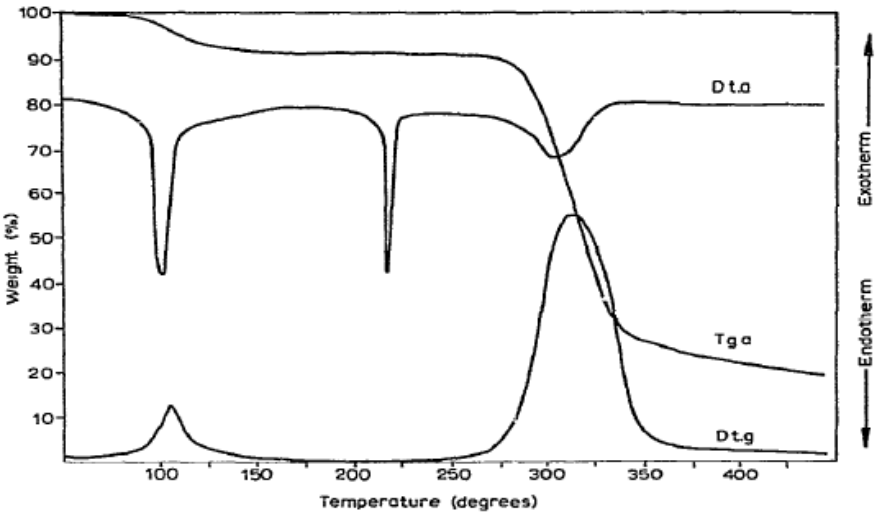


Figure 2-5: Thermogram from DTA and TGA of trehalose dihydrate (Shafizadeh and Lai, 1973)

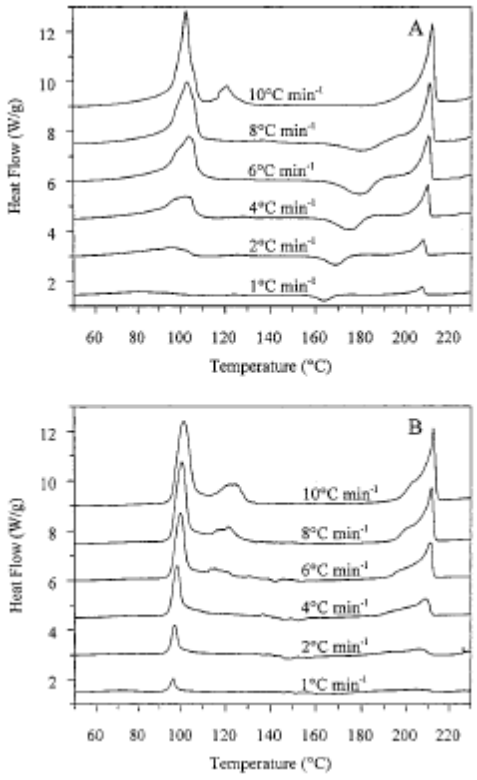


Figure 2-6: Influence of heating rate on DSC profile of (A) <45um particle size and (B) >450um particle size (Taylor and York, 1998)

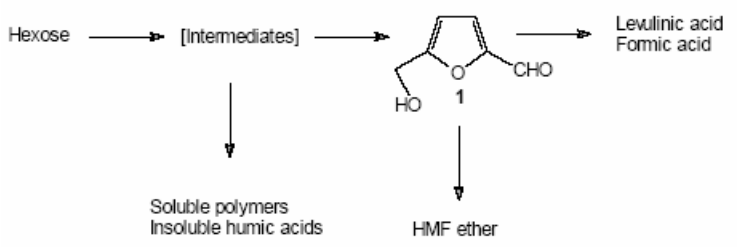


Figure 2-7: High level schematic of the early stages of decomposition of a hexose (Lewkowski, 2001)

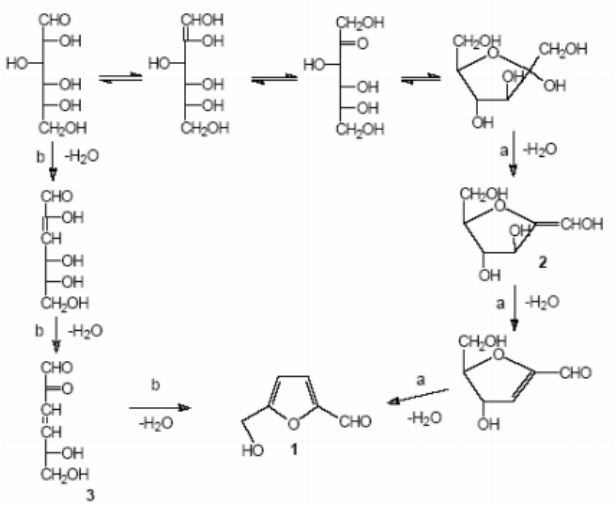


Figure 2-8: Two dehydration pathways for hexoses (Lewkowski, 2001)

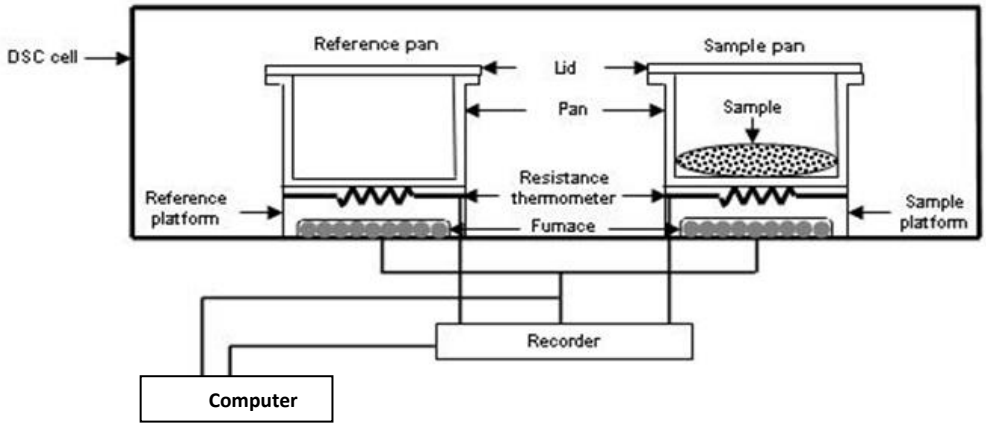


Figure 2-9: A schematic of power compensation DSC (Lee, 2010)

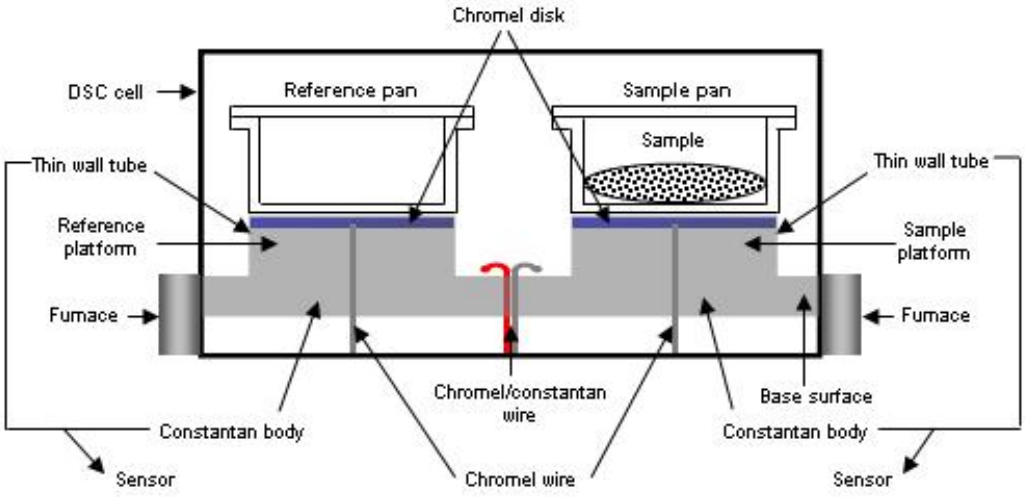


Figure 2-10: A schematic of heat-flux DSC (adapted from Danley 2003)

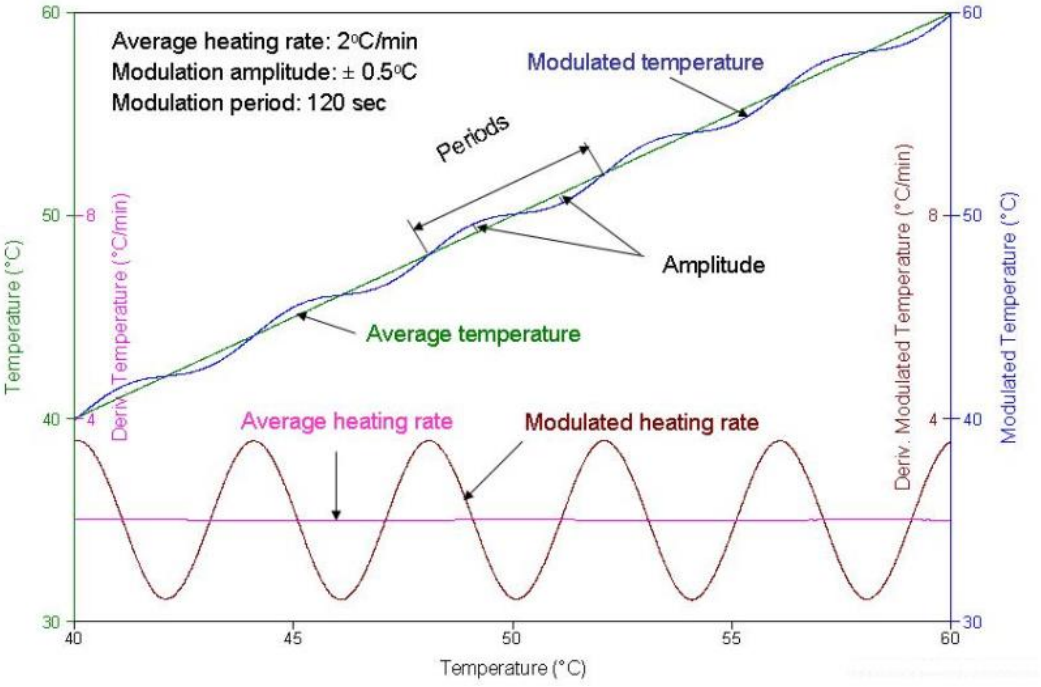


Figure 2-11: Plot showing the temperature modulation amplitude and period, average heating rate, and modulated heating rate used in MDSC Plots showing the temperature modulation amplitude and period, average heating rate, and modulated heating rate used in MDSC (Lee 2010).

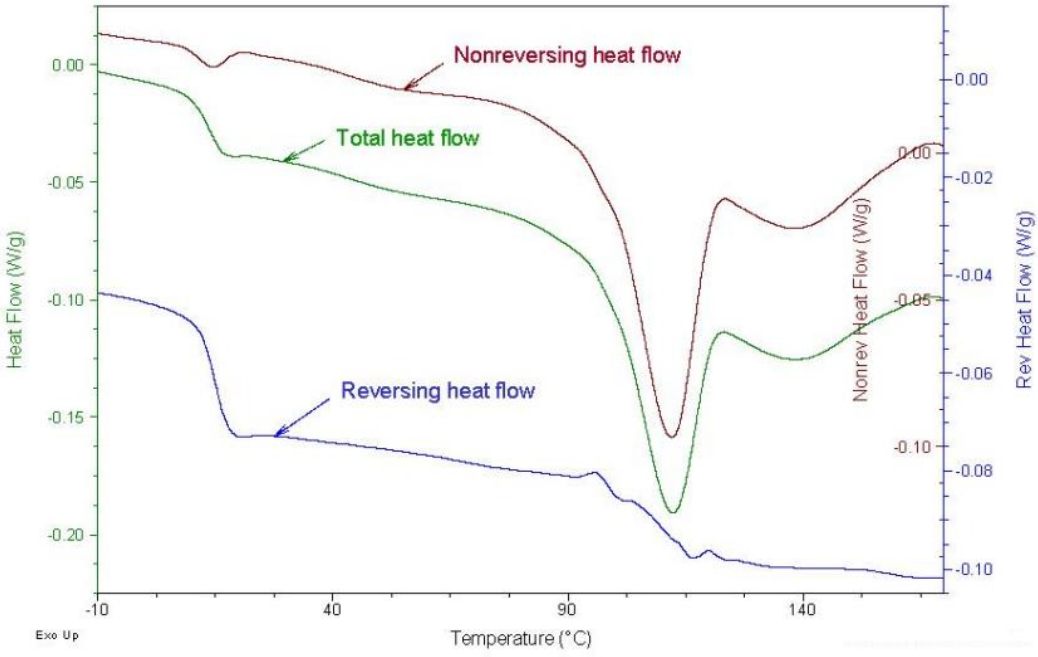


Figure 2-12: Total heat flow, reversing heat flow and nonreversing heat flow shown in the MSDS thermogram for fructose candy amorphous (Tg) and crystalline phases (Tm) (Lee 2010)

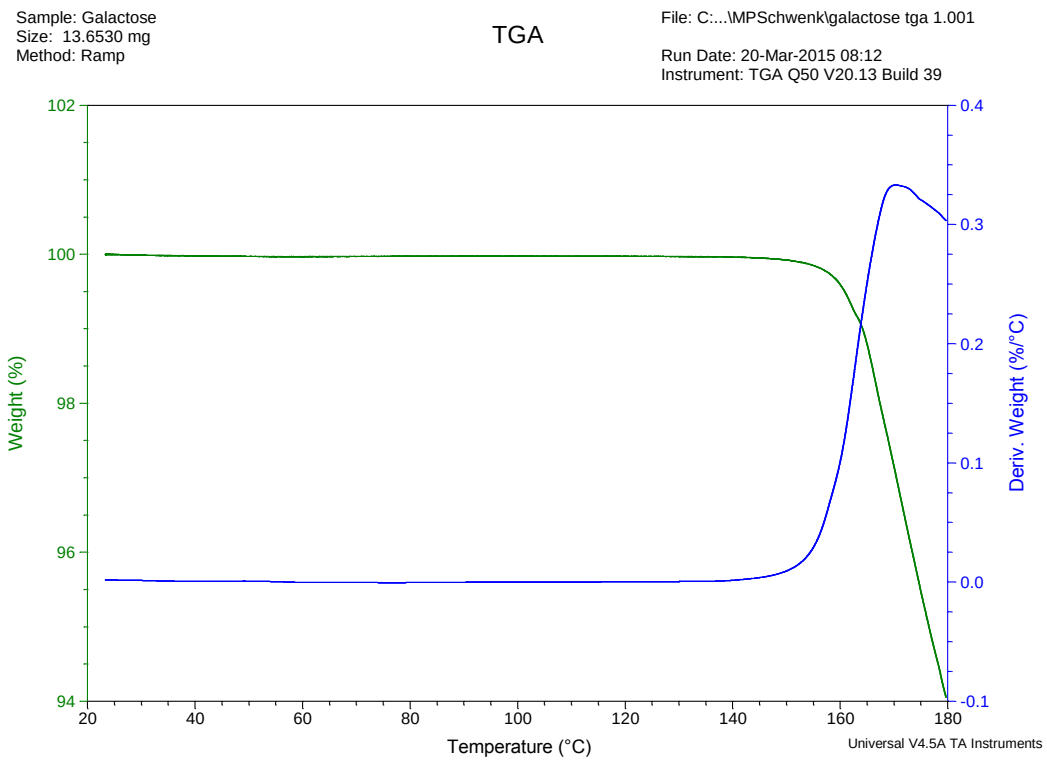


Figure 2-13: TGA of galactose at a heating rate of 1C/min showing the percent weight loss and the derivative of the percent weight loss

Tables

Table 2-1: Summary of monosaccharides and their resulting disaccharide combinations

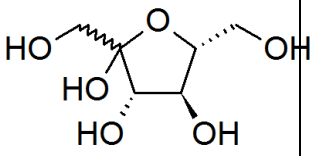
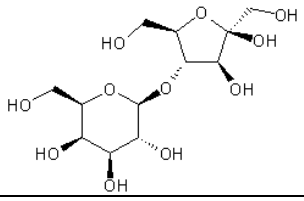
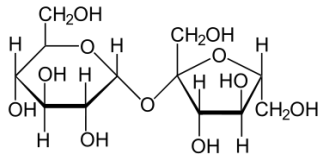
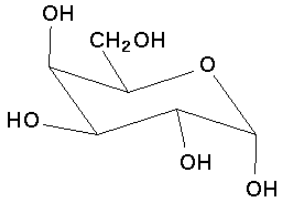
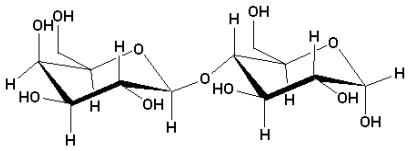
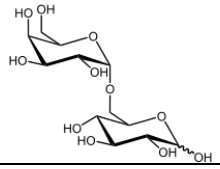
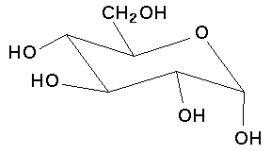
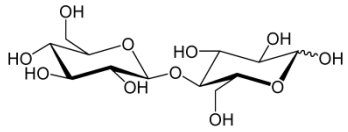
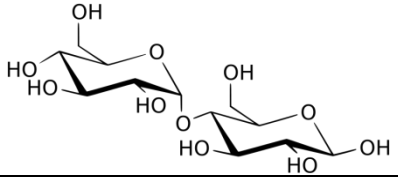
	Fructose	**Galactose**	**Glucose**
Fructose 		Lactulose 	Sucrose 
Galactose 	Lactulose		Lactose  Lactose Melibiose 
Glucose 	Sucrose	Lactose, Melibiose	Cellobiose  Maltose 

Table 2-2: Saccharides and their corresponding sugar alcohols (adapted from (Billaux et al., 1991))

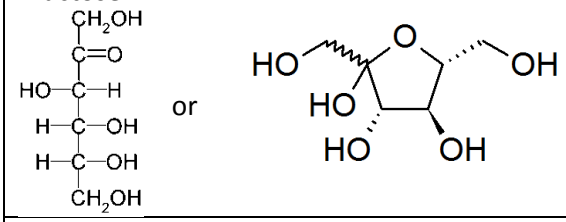
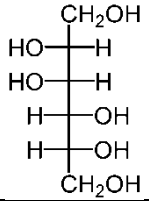
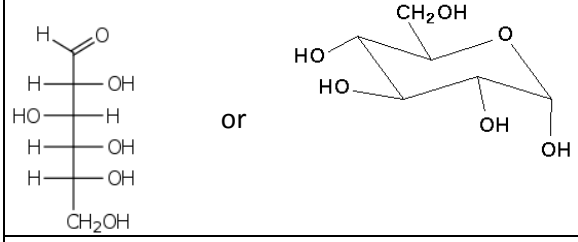
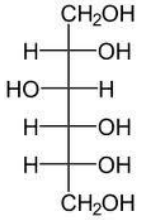
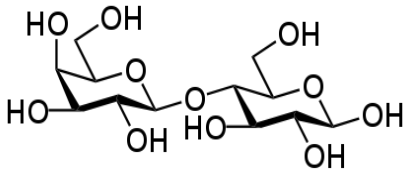
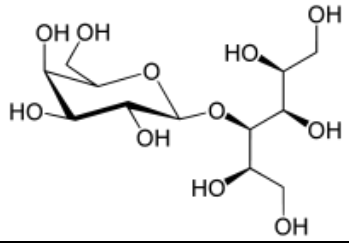
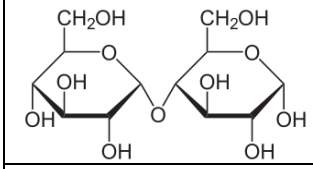
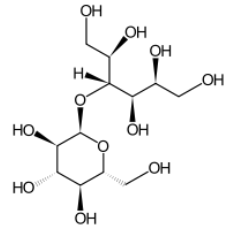
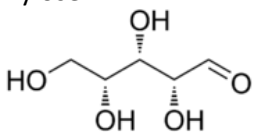
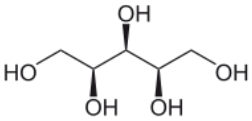
Saccharide	Corresponding Sugar Alcohol
Fructose 	Mannitol 
Glucose 	Sorbitol 
Lactose 	Lactitol 
Maltose 	Maltitol 
Xylose 	Xylitol 

Table 2-3: Comparison of thermodynamic versus apparent melting properties excerpted from Lee et al. (2011a)

Thermodynamic Melting	**Apparent Melting (caused by thermal decomposition)**
Similarities	
Loss of crystalline structure Produces an endothermic peak	
Differences	
– A single temperature	– Temperature depending on heating rate
– Time-independent	– Time-dependent (kinetics)
– Constant ΔH (amorphization enthalpy at constant T)	– Variable ΔH (amorphization enthalpy dependent on heating rate plus decomposition)
– No chemical alteration in material's molecules (pure crystalline material = pure liquid material)	– Chemical alteration in material's molecules (pure crystalline material ≠ pure liquid material)
Cause: phases have equal Gibbs energy (ΔG=0)	Cause: kinetic process, e.g. thermal decomposition

Table 2-4: Comparison of melting temperature by apparatus (Hurtta et al., 2004)

Sample	MP Apparatus	DSC	
	Melting Point °C	Onset Temperature	Peak Temperature °C
Sucrose A	179.7±0.2	173.7±1.6	176.6±0.1
Sucrose B	186.8±0.5	184.5±0.8	186.6±1.0
Glucose A	148.6±0.3	149.8±0.1	151.7±0.2
Glucose B	146.4±3.4	146.5±0.6	149.3±0.7
Fructose A	103.8±0.4	113.6±2.6	118.4±0.2
Fructose B	103.2±0.2	112.7±0.7	116.7±0.0

Three parallel measurements were done for each sample (except for ten parallel measurements for glucose B), and the average values were calculated. The onset and peak temperatures at DSC heating rate of 1°Cmin^{-1} are listed for comparison.

Table 2-5: Results of DSC and TG measurements for sucrose at different rates of heating (Hurtta et al., 2004)

Rate of heating (°Cmin^{-1})	Onset °C	Peak °C	ΔHf (Jg^{-1})	Ti °C
Sucrose A				
0.5	167.9± 1.3	169.9± 0.6	54.8±7.8	159.6
1	173.7±1.6	176.6±0.1	72.1±5.6	161.1
2	178.2±1.6	181.4±1.1	111.4±8.8	169.6
10	185.9±1.0	190.5±0.2	126.4±0.4	179.9
20	187.5±0.2	191.9±0.3	130.8±0.4	192.2
50	188.3±0.5	193.7±0.3	136.9±0.3	207.5
100	189.0±0.4	196.1±0.5	143.2±0.6	235.3
Sucrose B				
0.5	181.4±0.3	182.7±0.5	119.8±2.6	167.0
1	184.5±0.8	186.6±1.0	126.6±2.3	171.3
2	187.1±0.1	189.3±0.1	128.0±1.0	178.8
10	188.9±0.0	191.5±0.1	134.4±1.2	189.2
20	189.6±0.5	192.9±0.8	135.4±2.0	200.7
50	191.1±1.5	196.1±2.4	138.8±1.1	214.9
100	190.8±0.5	196.5±0.6	145.4±0.5	228.4
Glucose A				
0.5	147.5±0.2	149.1±0.2	182.7±2.0	146.4
1	149.8±0.1	151.7±0.2	189.1±1.2	149.8
2	152.8±0.4	154.8±0.4	189.0±1.5	151.4
10	160.4±0.7	163.1±0.0	195.9±1.2	166.4
20	164.8±0.0	167.4±0.1	200.1±2.0	176.5
50	169.4±0.0	172.6±0.1	208.0±0.5	191.6
100	171.8±0.5	176.1±0.6	220.7±3.6	194.4
Glucose B				
0.5	145.1±0.7	147.5±0.6	180.1±2.1	147.0
1	146.5±0.6	149.3±0.7	185.4±1.8	152.0
2	148.9± 1.3	151.9± 1.1	187.1±2.4	159.1
10	155.2±0.6	159.4±0.5	194.3±1.4	170.3
20	158.3±0.8	163.8±1.0	199.1±0.5	183.5
50	163.3±0.7	168.9± 0.3	206.9± 1.0	201.1
100	166.7±0.8	173.8±1.3	218.9± 1.9	204.3
Fructose A				
0.5	108.2±2.6	114.3±0.6	147.6±0.3	110.7
1	113.6±2.6	118.4±0.2	156.0±1.8	116.3
2	112.0±1.6	123.2±0.4	161.5±1.3	122.8
10	125.8±0.2	134.1±0.0	174.8±4.4	138.7
20	131.3±0.3	137.8±0.2	185.9± 3.3	145.0
50	135.7±0.2	140.6±0.4	197.8±2.2	161.6
100	137.0±0.1	142.6±0.1	212.8±1.5	166.1

Table 2-5 (cont.)

Rate of heating (°Cmin^{-1})	Onset °C	Peak °C	ΔHf (Jg^{-1})	Ti °C
Fructose B				
0.5	110.0±1.0	113.0±1.0	151.6±0.7	110.4
1	112.7±0.7	116.7±0.0	154.1±4.0	113.9
2	116.2±0.6	121.0±0.2	163.9± 1.6	119.0
10	125.7±0.8	131.7±0.3	176.7±2.8	136.8
20	130.0±0.2	136.0±0.2	185.5±1.3	147.1
50	134.9±0.1	139.8±0.4	199.2±3.9	157.0
100	136.8±0.4	142.0±0.5	203.7±3.2	165.4

Table 2-6: Results of sucrose melting temperature from Beckett et al. (2006)

		T1°C	**T2°C**	**ΔH1(J/g)**	**ΔH2(J/g)**
Sucrose	FC	154.3±0.2	190.5±0.3	1.1±0.1	116.0±1.3
	T&L	154.4±0.1	190.9±0.1	0.9±0.1	122.0±0.8
	SP	No results given	192.4±0.2	No results given	131.4±1.6
	L	No results given	191.7±0.1	No results given	132.8±1.4
Recrystallized	FC	154.3±0.2	180.8±0.1	33.3±0.8	85.4±0.7
	T&L	154.4±0.1	182.2±0.2	17.1±0.6	101.0±1.2
	SP	No results given	190.0±0.1	No results given	119.3±0.5
	L	154.3±0.2	186.8±0.3	3.9±0.3	108.5±0.3

Table 2-7: Main peaks observed in DSC in etamsylate, fluconazole and lactose and mixtures of each. The temperatures are showed aligned to visually see similarities and differences. (Desai et al., 2003)

Material Analyzed by DSC	Peak Temperature/°C				
Etamsylate	___	___	136.7	___	___
Fluconazole	___	___	___	140.4	___
Lactose	___	___	___	___	145.0 (exotherm)
Etamsylate:Lactose (1:1)	___	118.5	131.4	___	___
Fluconazole:Lactose (1:1)	86.1	___	136.4	140.2	___

Table 2-8: Melting temperature and enthalpy values summary from Roos (1993)

Compound	Tf(°C)[a]			ΔHf (J/g)[a]		Tf /Tg[a]	
	I	II	III	I	II	I[e]	III
D-Arabinose	150(160)			238		1.56(1.60)	
D-Ribose	70(86)	60(90)	87	146	150	1.36(1.42)	1.37
D-Xylose	143(157)	135(150)	153	211	280	1.49(1.54)	1.51
D-Fructose	108(127)	80(115)	124	169	180	1.37(1.44)	1.06
α-D-Fucose	133(145)	115(130)		186	190	1.36(1.40)	
D-Galactose	163(170)	140(165)	170	243	280	1.44(1.46)	1.16
D-Glucose	143(158)	135(150)	158	179		1.37(1.42)	1.42
D-Mannose	120(134)		139.5	137		0.32(1.37)	1.36
α-L-	86(99)	85(100)		191	210		
L-Sorbose	153(163)	140(160)		245	250	1.46(1.49)	
α-Lactose[b]	(214)	160(195)				(1.30)	
Maltose[b]	104(123)		129[f]	126		1.27	
α-Melibiose[c]	138						
Sucrose	173(190)	160(185)	192	118	120	1.33(1.35)	1.43
α-α-	91(97)		203	127			1.35
Maltitol	139(149)	115(150)		147	150	1.32(1.35)	
D-Glucitol	85(99)	60(95)	111	154	150	1.36(1.41)	1.42
Xylitol	89(95)	65(100)	94	226	250	1.48(1.51)	1.44

[a] I, This Study; II Raemy and Schweizer (1983); III Slade and Levine 1991; [b] Monohydrate; [c] 0.5 mol H_2O/mol.; [d] Dihydrate. [e] Values calculated with onset values of Tf and Tg; values in parentheses are those calculated with peak values of Tf and onset values of Tg. [f] Anhydrous

Table 2-9: Comparison of fusion temperatures, enthalpies and entropies of various sugar alcohols (adapted from Barone et al. (1990)

Compound	Phase Change	No. of	T/K		ΔH/kJ mol $^{-1}$		ΔS/J mol^{-1}K^{-1}
			Barone et al. (1990)	Lit value	Barone et al. (1990)	Lit value	
meso-pentaerythritol	Fusion	4	390.9	391.6[a]	39.4(0.2)	42.3[a] ,41.8[b]	100.8(0.5)
	Transition	7	458.3 (0.4)	460[d] 57[e]	40.5(0.3)	44[d], 41[e], 8.7[f]	88.4(0.6)
	Fusion	4	513.2(0.6)	538.7[d]528[e]	4.6(0.3)	7.1[d], 5.0[e]	9.0(0.6)
adonitol	Fusion	4	374.7(0.2)	375[g] 374[h]	37.6(0.1)	38[c]	100.3 (0.3)
D-arabinitol	Fusion	4	379.4(0.1)	376[g]	38.9(0.2)	---	102.5(0.5)
xylitol	Fusion	4	365.7(0.1)	367[g]	37.4(0.3)	38	102.3(0.8)
dulcitol	Fusion	6	460.3(0.1)	459-61[g]	65.1(0.6)	60.1[c]	141.4(1.3)
D-mannitol	Fusion	7	439.1(0.1)	439[a,b]	56.1(0.3)	53.6[a], 52.8[c]	127.8(0.6)
D-sorbitol	Fusion	4	366.5(0.3)	367.5(B) [l]361.3(A)[l]371.9(Γ)[l]	30.2(0.4)	31.5(B)[l]34.3(A)[l] 34.3(Γ)[l]	82.5(1.1)
myo-inositol	Fusion	7	469.9(0.1)	498-99[g]	47.9(0.4)	46.8[c]	96.4(0.8)

Standard deviation in brackets. [a] Spaght 1932; [b] Nitta et al. 1950; [c] Raemey and Schweizer 1983; [d] Nitta et al. 1950a; [e] Murrill and Breed 1970; [f] Mayer 1987; [g] *Handbook of Biochemistry and Molecular Biology,* ed. G. D.Fassman (CRC Press, Cleveland, USA, 1975) [h] Schwartz et al. (1972), [i] Quinquenet et al. (1988)

Table 2-10: Summary of main degradation peak from GC (Räisänen et al., 2003)

Sugar	Main Peak in Chromatogram
Pentose (Arabinose, Xylose)	2-furancarboxaldehyde
Hexose (Mannose)	(2H)-furan-3-one
Arabinitol	Furan methanol (at 500°C)

Table 2-11: Ratios of xylose anomers at various temperatures (Shafizadeh et al., 1971)

Temp. °C	α- D- Xylopyranose, %	β-D-Xylopyranose, %
25	90.6±4.0	9.4±4.0
127	91.7±0.6	8.3±4.0
131	85.9±2.1	14.1±2.1
140	83.0±0.4	17.0±0.4
149	73.0±0.7	27.0±0.7
154	47.9±0.3	52.1±0.3
200[a]	48.0	52.0

[a] This sample showed 5.3% weight loss due to condensation. The ratio of anomeric forms was determined by the analysis of the remaining free sugar.

Table 2-12: Kinetic information on the decomposition of xylose obtained by the gas chromatographic method (Tanaka and Nakamura 1983)

Heating Temp °C	Order of Reaction	Rate Constant κ	Ln A
160	1.4	5.629×10^{-4}	27.35
170	1.6	1.058×10^{-3}	27.20
180	1.7	2.499×10^{-3}	27.30
190	1.8	4.840×10^{-3}	27.25
200	1.8	1.044×10^{-2}	27.33

Table 2-13: Values of onset, peak, and enthalpy from DSC and decomposition from TG in xylose (Lappalainen et al., 2006)

Heating Rate K min^{-1}	Onset °C	Peak °C	$\Delta Hf_{/}J\ g^{-1}$	Tf °C
L-xylose				
0.5	143.9	147.3	208	145.1
1	147.1	150.5	213	146.9
2 (non-dried)	150.0	153.8	229	---
2	151.4	155.3	222	149.2
10	155.8	160.8	237	164.5
20	159.2	164.8	251	198.0
40	162.2	168.4	251	187.5
D-xylose				
0.5	136.8	142.4	207	138.5
1	139.7	145.8	216	147.0
2 (non-dried)	142.6	149.6	217	----
2	143.7	150.1	222	147.1
10	152.8	157.7	228	160.7
20	156.3	162.7	236	174.0
40	158.3	166.3	239	184.4

Table 2-14: Signals obtained from MDSC and their associated calculation (Lee 2010)

Signals	Type of signal	Calculation
Total heat flow	Measured signal	The average value of the modulated heat flow Heat flow signal at the average heating rate
Rev heat flow	Calculated signal	Rev C_p x average heating rate
Non-rev heat flow	Calculated signal	Total heat flow - Rev heat flow
Total C_p	Calculated signal	Total heat flow x KC_p Total / average heating rate (KC_p Total: Calibration constant for Total C_p, which is obtained by heat capacity calibration)
Rev C_p	Calculated signal	Heat flow amplitude x KC_p Rev/ heating rate amplitude (KC_p Rev: Calibration constant for Reversing C_p, which is obtained by heat capacity calibration)
Non-rev C_p	Calculated signal	Total C_p – Rev C_p

Table 2-15: Signals obtained from quasi-isothermal MSDC (Lee 2010)

Signals	Calculated?	Calculation
Total heat flow	Yes (Measured signal)	The average value of the modulated heat flow The heat flow signal at the average heating rate
Rev heat flow	No	Average heating rate = 0
Non-rev heat flow	No	Rev heat flow cannot be calculated due to average heating rate = 0
Total C_p	No	Average heating rate = 0
Rev C_p	Yes	The heat flow amplitude and heating rate amplitude required to calculate Rev C_p depend on modulated heating rate, which results from a modulated temperature amplitude and a modulated temperature period.
Non-rev C_p	No	Total C_p cannot be calculated because average heating rate = 0

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CHAPTER 3

Screening of Heating Rate Dependence of the Loss in Crystal Structure in Carbohydrate Materials by Differential Scanning Calorimetry (DSC)

Abstract

Twenty-five carbohydrate type materials were screened using DSC to characterize the heating rate dependence of their melting temperature. Three heating rates were used: 1, 5 and 25°C/min. Based on previous work, it was hypothesized that if the material had the same melting onset temperature (Tm onset) regardless of heating rate, the material was classified as a thermodynamic melting material. Five compounds (erythitol, maltitol, mannitol, sorbitol and xylitol) had exhibited little to no change in Tm onset regardless of heating rate and were classified in the no/low heating rate dependency group. The eleven compounds (D and L arabinose, fructose, glucose anhydrous, glucose monohydrate, lactose anhydrous, lactose monohydrate, maltose, sucrose, trehalose and xylose) that exhibited a very large difference in Tm onset (greater than 10°C) between the lowest (1°C/min) and highest heating rate (25°C/min) were classified in the high rate dependency group and were considered to be apparent melting materials. The remaining compounds (citric acid, galactose, lactitol, lactulose, mannose, raffinose, ribose, and tagatose) exhibited a Tm onset difference of 2 to 10°C between the lowest and highest heating rates and were classified in the medium heating rate dependency group. Further investigation of the materials in the medium heating rate dependency group will need to be done in order to understand more conclusively their thermal behavior and to determine if they are apparent melting or thermodynamic melting materials. A shift in peak onset temperature with heating rate is a function of the activation energy of the process causing the shift. Therefore, each material can show a different shift. High activation energy results in a small shift while low activation energy results in a large shift.

Introduction

Melting point has long been a characteristic measurement parameter used for compound identification. Melting is a first order phase transition from the crystalline phase to the liquid phase (Roos, 1995; Wunderlich, 1990). Thermodynamic melting occurs at a single, time-independent (i.e., heating rate independent) temperature (most often reported as $T_{m\ onset}$), where the crystalline solid and corresponding liquid phases are in thermodynamic equilibrium at a constant pressure; that is, the

temperature at which the Gibbs energy (G; also called free enthalpy) of the crystalline solid phase is equal to that of the corresponding liquid phase, $\Delta G=0$ (Wunderlich, 1990). Melting is characterized by three parameters: Tm onset: onset melting temperature; Tm peak: peak melting temperature; and ΔH: enthalpy of melting. Recent studies by Lee et al. (2011a) defined a new type of melting termed "apparent melting". In apparent melting, the loss of crystalline structure is due to a kinetic process, such as thermal decomposition, rather than thermodynamic melting. Since the melting temperature of these materials is being influenced by a kinetic event, the Tm onset (onset of melting) is heating rate dependent. Three carbohydrate materials (sucrose, fructose, and glucose) investigated by Lee et al. (2011a) exhibited this type of melting, and were identified as apparent melting materials. In the same research, one carbohydrate type compound, mannitol, a sugar alcohol, was shown to exhibit a heating rate independent Tm onset. This type of melting was termed thermodynamic melting. Lee et al. (2011b) demonstrated via HPLC that decomposition products are detectable in sucrose at temperatures below its melting temperature. In the case of fructose and glucose, HPLC determination of decomposition products was not done.

DSC is one of the thermal analysis techniques that measures the heat flow difference between a sample and an inert reference (typically an empty pan). Integration of the signal provides enthalpy (H), which is a function of the specific heat of the material (Cp) and the amount of energy absorbed or released by the phase transition of the material. As Lee et al. (2011a) pointed out; the DSC makes two important characteristics of thermodynamic behavior visible:

1. At any given temperature there is an absolute difference in enthalpy (H, J/g) between the crystalline and amorphous phases.
2. This difference increases with increasing temperature due to the difference in heat capacity between the two phases.

These two points show that in thermodynamic melting materials there should be no difference in ΔH (J/g) between the crystalline and amorphous phases. The enthalpy should be a single constant value equal to the area of the endothermic peak. The ΔH should be independent of time (i.e. independent of heating rate).

Hurtta et al. (2004) and Lappalainen et al. (2006) reported in their research on sucrose, glucose, fructose (Hurtta et al., 2004) and xylose (Lappalainen et al., 2006) that the Tm onset heat rate dependence was due to thermal decomposition and maturotation (with the exception of sucrose) in addition to melting. In regards to maturotation, Lee et al. (2011a) pointed out that mutarotation in

crystalline sugars should be initiated only after melting begins (Wlodarczyk et al., 2009). Maturotation should affect only the shape of the melting peak after the onset of melting, but not the onset temperature.

When comparing results between different apparatus, it is important to consider the thermal lag between the temperature measured and the temperature of the sample. For example, in Thermal Gravimetric Analysis (TGA) the temperature probe is not in direct contact with the sample but rather, is suspended above the sample. The difference in distance between the sample and the probe causes a thermal lag between the temperature measured by the probe and the sample. The difference in temperature (thermal lag) is greater at higher heating rates. When comparing the temperatures of the onset of melting to the temperatures of the onset of decomposition, thermal lag needs to be taken into consideration.

The idea of apparent melting has caused much discussion in the literature. Roos et al. (2012) published some objections to the initial papers by Lee et al. (2011a) and Lee et al. (2011b) defining apparent melting. The objections included the authors not considering the following issues:

1. Effects of residual or produced water
2. Water evaporation can produce a large endothermic shift in heat flow
3. Crystals time dependently dissolve (instead of melting)
4. Decomposition products were not detected visually in the initially melted samples

Schmidt et al. (2012) offered comments in their rebuttal paper and clarified the data in contrast to the position of Roos et al. (2012). For instance, if residual water were the issue (1), then mannitol would show a similar problem because mannitol had the highest water content of the materials tested. To contrast with the suggestion concerning water evaporation (2), water was not lost, and the samples' pan weight was not changed during the heating of the pans in the DSC. The dissolve/melt hypothesis laid out by Roos et al. (2012) (3) could be the mechanism for decomposition which would not negate the work of Lee et al. (2011a) since they did not suggest a mechanism. In regards to the assertion that decomposition products were not seen, Schmidt et al. (2012) showed that decomposition products are detected in the HPLC before a color change is "seen" in the samples. Thus, detection of decomposition products by HPLC would be a more accurate determination of decomposition than color development.

Further explanation of the melting and decomposition at low temperatures for long times was given by Roos et al. (2013). Here the authors further asserted that these behaviors could be accounted for by impurities and defects. Amorphous regions and melted regions were asserted to be necessary for

decomposition to take place. Looking again at the decomposition schematic for a monosaccharide, the reactions are intramolecular (dehydration reaction), and therefore could take place within the lattice structure. For disaccharides, the first reaction is a hydrolysis of the glyosidic bond, which also could take place within the crystal lattice. Since the reactions are intramolecular, it may not require a high degree of mobility in order for the reaction to take place.

Each of the three sugars (fructose, glucose, sucrose) tested by Lee et al. (2011a) showed apparent melting behavior, and the polyol mannitol tested did not. Trying to understand and draw general conclusions from the four materials used in the Lee et al. (2011a) research is difficult. Sucrose is a disaccharide, whereas fructose and glucose are monosaccharides. Sucrose is the disaccharide that is composed of fructose and glucose. Fructose is a 6-carbon sugar (hexose) and is called a furanose, since it usually exists as a 5-carbon ring. Glucose is a 6-carbon sugar called a pyranose since it has a 6-carbon ring. Both glucose and fructose are reducing sugars, whereas sucrose is not (El Khadem, 1988). Mannitol is a monosaccharide that has been reduced; it no longer has a carbonyl group, but instead has a hydroxyl group. It is nearly impossible to gain an understanding of trends or patterns between thermodynamic and apparent melting materials using only four materials.

Mathlouthi and Roge (2012) points out that the structural aspect of compounds is frequently neglected when trying to understand melting points of sugars. They point out that the loss of crystalline structure in the case of carbohydrates occurs due to the breakage of inter- and intra-molecular hydrogen bonds. They suggest that comparison of hydrogen bonding in polyols and sugars can explain differences in their melting behavior. Considering other groups of carbohydrate type compounds are needed to further the understanding of the intermolecular hydrogen bonds and how they relate to the melting temperature of sugars. More information is needed on other carbohydrate materials to understand better what is happening to the samples when heating occurs and to draw conclusions between the different types of carbohydrate compounds.

Thus, the objective of this research is to screen materials based on molecular weight and reducing capacity, and to begin the exploration of other crystalline carbohydrate type materials in addition to sucrose, glucose, fructose, and mannitol for thermodynamic or apparent melting behavior. Screening occurred using the DSC to identify compounds that exhibit heating rate dependent Tm onset and/or ΔH values. Information on more materials added to our knowledge of the behavior of different carbohydrates and added to the understanding of what is occurring when carbohydrate compounds are heated. Monosaccharides and disaccharides were tested, as well as polyols. Citric acid was included in

this study as a material with similar functional groups as sugars and polyols, but which is neither a polyol nor a sugar. The sugars have one carbonyl group per monosaccharide unit and a hydroxyl group per carbon. The citric acid possesses a carboxylic acid (carbonyl group and a hydroxyl on the same carbon), as well as hydroxyl groups. Xylitol is completely reduced so it has only hydroxyl groups (one per carbon).

Materials and Methods

Materials

Screening work involved testing 25 types of simple carbohydrate materials including mono- and disaccharides, poylols, and acids listed in Table 3-1.

Sources of the above materials are listed in Table 3-1 along with chemical abstract service (CAS) numbers, and purity as reported by the supplier. Table 3-2 records the number of carbons and the molecular formula of the materials tested in this experiment. The list includes sugars with 4 to 12 carbons, reducing and non-reducing sugars, and sugar alcohols. Citric acid was also tested as a related crystalline carbohydrate material.

Methods

Standard DSC (SDSC) and stepwise quasi-isothermal MDSC experiments were carried out using a DSC Q2000 (TA instruments, New Castle, DE), equipped with a Refrigerated Cooling System (RCS 90). Ash content was analyzed using the sulfated ash method (Corn Refiners Association Method M-4) and is reported in Table 3-2. Moisture content was determined by coulometric Karl Fischer titration using Hydranal Coulomat AG (methanol based anolyte) as the solvent.

Standard DSC (SDSC) experiments

The DSC Q2000 (TA instruments, New Castle, DE) was calibrated for enthalpy (cell constant) and temperature prior to sample measurements. Temperature calibration was performed to correct the difference between the known melting temperature of a standard (indium, $T_{m\ onset}$ of 156.6^{o}C, ΔH of 28.71 J/g, Lot# A10R020, TA instruments, New Castle, DE) and its measured melting temperature. Hermetic Anodized, Aluminum Pans and lids (TA instruments, New Castle, DE) were used for all calibration and sample measurements, including an empty pan as the reference. Dry nitrogen, at a flow rate of 50 mL/min, was used as the purge gas.

Hermetically sealed samples (approximately 2.75 mg) were equilibrated at 25^{o}C and then heated at heating rates of 1, 10, and 25^{o}C/min over the temperature range where an entire endothermic peak was obtained. All samples were measured in triplicate at each heating rate. Universal Analysis (UA) software (TA instruments, New Castle, DE, version 4.4A) was used to plot the average heat flow signal of triplicate measurements at each heating rate against temperature. Melting parameters (Tm onset, Tm peak, and ΔH) were obtained from the DSC thermograms using the TA Universal Analysis software and are in Table 3-3.

A delta onset temperature (ΔTm onset) and a delta peak temperature (ΔTm peak) were calculated by subtracting the melting temperature values obtained at rate of 1°C/min from the rate obtained at 25°C/min. The results are given in Table 3-3. Three replicates were done for each heating rate, and three integration analyses of each run were performed using the sigmoidal tangent method. Standard deviations were calculated on each sample run for each set of analyses. These values were then averaged to obtain the standard deviation for each carbohydrate material. This method to calculate standard deviation was chosen rather than a calculation, which weighed all the results equally, since the variance between measurements should be considered different than the variance between samples run.

Results and Discussion

Standard DSC (SDSC) experiments

SDSC experiments were performed in order to explore the heating rate dependency of the melting parameters (Tm onset, Tm peak, and ΔH) for the select materials. Table 3-3 shows the results of the melting parameters for the compounds studied including the Tm (onset), Tm (peak), and enthalpy of each of the three heating rates. Comparing these values to the literature values is difficult due to the variation in literature values for many of the compounds as seen in Table 3-2. Further complications can occur for some materials when viewing the large differences found in the literature reported heating rate at which the melting temperature was measured. Table 3-4 summarizes the range of literature values and the range of values obtained by DSC at different heating rates reported in this work, demonstrating good agreement between the two.

All the polyols screened fell into the no/low heating rate dependent onset group, except for lactitol. Mannitol thermograms are shown in Figure 3-1. Although the line is drawn at 2°C, all the compounds in the no/low heating rate dependency group actually exhibited less than 2°C ΔTm onset. The literature has consistently shown most polyols to exhibit stable melting parameters. Lappalainen et al. (2006) used xylitol (instead of a typical standard like Indium) to measure thermal lag in their experiments on L- and D-xyloses, noting that xylitol's melting behavior is normal. That is, it appears to be a thermodynamic melting material. Lee et al. (2011a) demonstrated mannitol as appropriate for use as comparison material more similar in nature to sugars than other standards like indium.

Lactitol exhibited a larger heating rate dependency compared to the other polyols investigated in this study. This larger heating rate dependency may be because lactitol is a monohydrate compound. Thus, the presence of water may be affecting its melting behavior. Other hydrates tested in this study include trehalose, which falls into the medium heating rate dependency group and maltose and glucose monohydrate that fall into the high rate dependency group.

The difference between the Tm (onset) and Tm (peak) at heating rates of 1 and 25°C/min are graphed in Figure 3-5. These results have been separated into three categories; dividing lines are shown at 2 and 10°C. The three heating rate dependency categories are: (1) small ΔTm onset <2°C, (2) medium ΔTm onset 2 to 10°C, and (3) large ΔTm onset >10°C. The limit of 10°C was determined using the ΔTm onset observed for sucrose, which has been previously shown to exhibit apparent melting behavior. Table 3-6 organizes the materials studied into the three heating rate dependent classifications.

The large heating rate dependent group definitely exhibits a heating rate dependent melting temperature. The challenge in the large heating rate dependent group is to verify that there is a kinetic event occurring at or before the melting temperature, which is causing the loss in crystalline structure. Similar increases in heating rate dependency were reported by Hurtta et al. (2004) and Lee et al. (2011a) studying sucrose, glucose, and fructose. Lee et al. (2011a) explained the differences in the magnitude of the heating rate dependency to the non-reproducible (non-uniform) nature of the kinetic process of thermal decomposition. Hurtta et al. (2004) suggested decomposition and mutarotation affected the melting temperature. The classification of this research further added xylose, lactose, and lactose monohydrate, arabinose, maltose and trehalose into the large heating rate dependent group. Average thermograms for xylose are shown in Figure 3-3 and for lactose monohydrate is shown in Figure 3-4. Both L- and D- arabinose were included in the study to determine if there was any difference in the Tm onset or the heating rate dependence between different stereoisomers. The high heating rate dependent group is apparent melting with a large dependency on a kinetic event influencing the loss of crystal structure.

The third group, the medium heating rate dependency group (2 to 10°C) contains the remaining compounds screened in this study, citric acid, galactose, lactitol monohydrate, lactulose, mannose, raffinose, maltose, ribose and tagatose. Understanding the medium heating rate dependency group of materials requires further investigation. The materials in the medium heating rate dependency group contain a range of ΔTm onset. A shift in peak onset temperature with heating rate is a function of the activation energy of the process causing the shift. Therefore, each material can show a different shift. High activation energy results in a small shift while low activation results in a large shift. Further work on decomposition onset, MDSC, and quasi-isothermal MDSC are needed to understand the thermal behavior of these materials.

Figure 3-6 is a plot of the change of enthalpy between the enthalpy of the melting endotherm at 25°C/min and the melting endotherm at 1°C/min. In general, one would expect an increase in enthalpy with an increase in heating rate for apparent melting materials. Lee et al. (2011a) noted that a characteristic of apparent melting is variable ΔH. The change in enthalpy is dependent on heating rate as well as decomposition. A characteristic in thermodynamic melting is constant ΔH or amorphization enthalpy at constant T. Enthalpy in a DSC peak in apparent melting materials is influenced by the loss of crystalline structure (or amorphization) enthalpy, as well as the enthalpy of the decomposition reaction. As the material is heated at a faster rate through the melting temperature range, more heat is applied,

causing more decomposition, causing a greater enthalpy. This variable enthalpy is seen in the results in Figure 3-6. In the case of lactose monohydrate, the large difference in enthalpy is also influenced by the endothermic peak caused by the loss of water, which at 25°C/min is unresolved from the melting peak, but can be separated at the rate of 1°C/min as can be seen in Figure 3-4.

Conclusions

The onset of melting showed high heating rate dependence for the D- and L- arabinose, fructose, glucose anhydrous, glucose monohydrate, maltose, sucrose, trehalose and xylose. These materials are all sugars, both mono and disaccharides. Based on previous work by Lee et al. (2011a), these materials should be classified as apparent melting materials. Heat rate had little to no effect on the melting temperature of erythitol, maltitol, sorbitol, and xylitol (no/low heat rate dependent group). These compounds would be interpreted to be thermodynamic melting (Lee et al., 2011b) and are all polyols. The onset of melting showed medium heating rate dependence in citric acid, galactose, lactitol, lactulose, raffinose, ribose, and tagatose (medium heat rate dependent group). The amount of dependence varied based on the samples, and further work would need to be done to make conclusions on the type of melting each material demonstrates. Further work will explore in detail selected materials in the medium heating rate dependent group. A detailed understanding of the thermal behavior of these materials will be observed using MDSC, quasi-isothermal MDSC and the TGA.

Figures and Tables Chapter 3

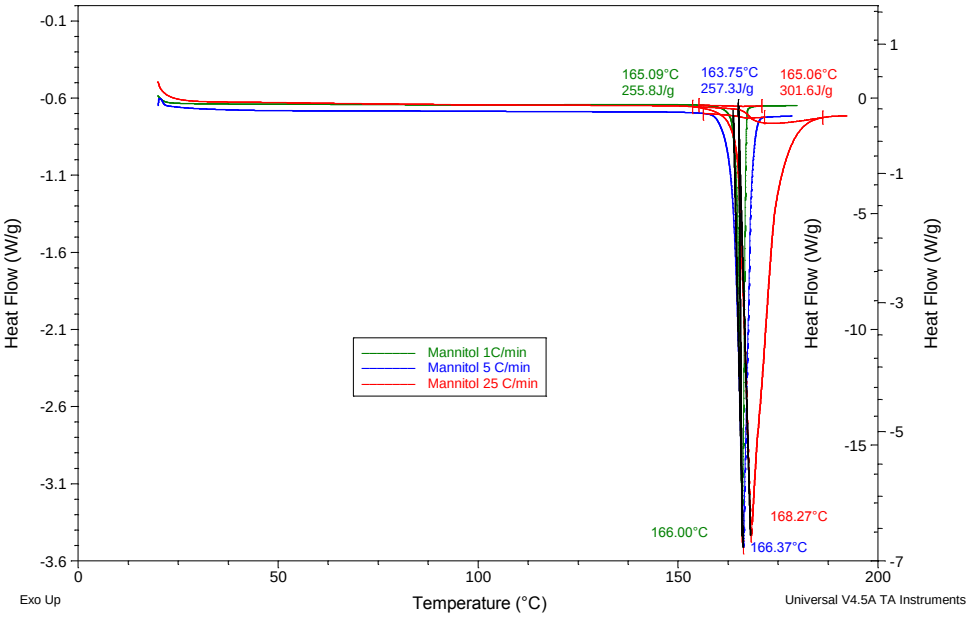

Figure 3-1: DSC thermograms of mannitol at 1, 5 and 25°C/min

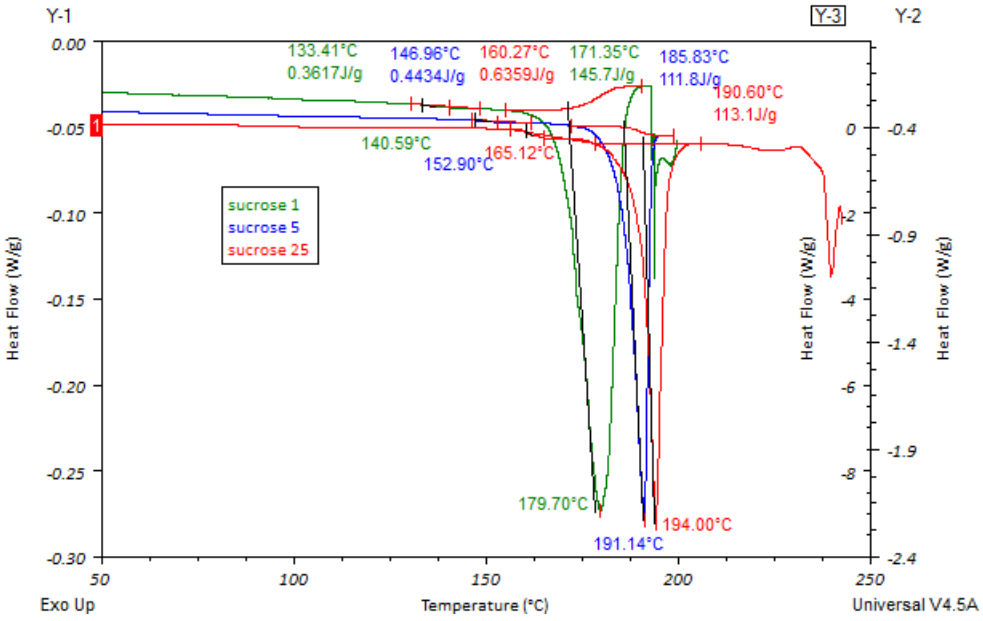

Figure 3-2: DSC thermograms of sucrose at 1, 5, and 25°C/min

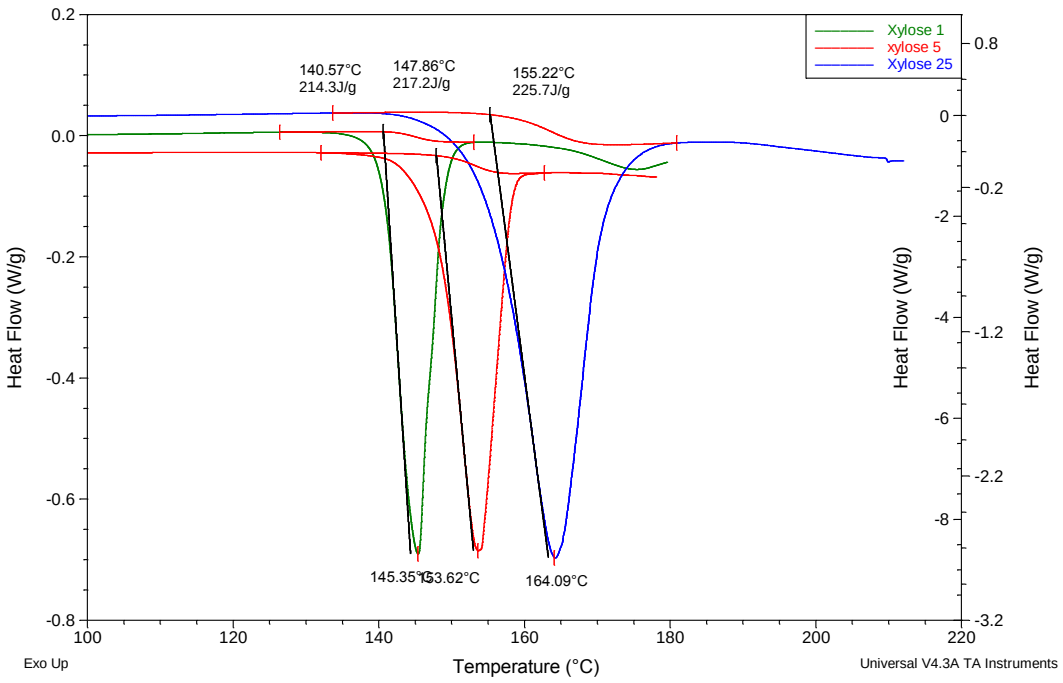

Figure 3-3: DSC thermograms of xylose at 1, 5, and 25°C/min

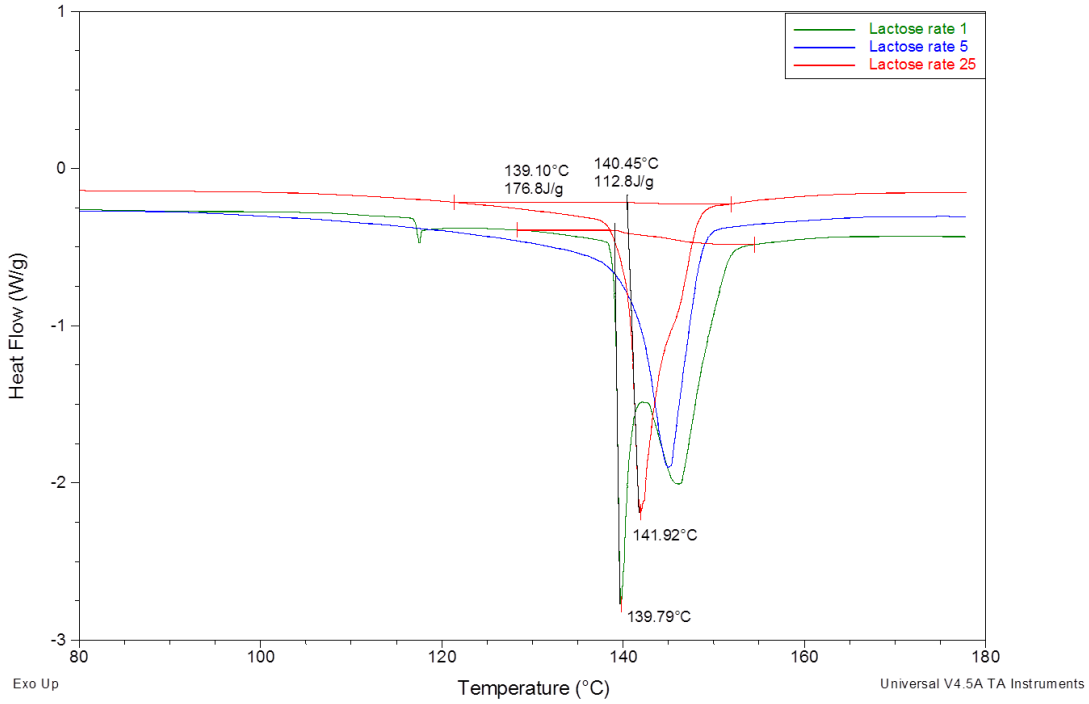

Figure 3-4: DSC thermogram of lactose monohydrate at 1, 5 and 25°C/min

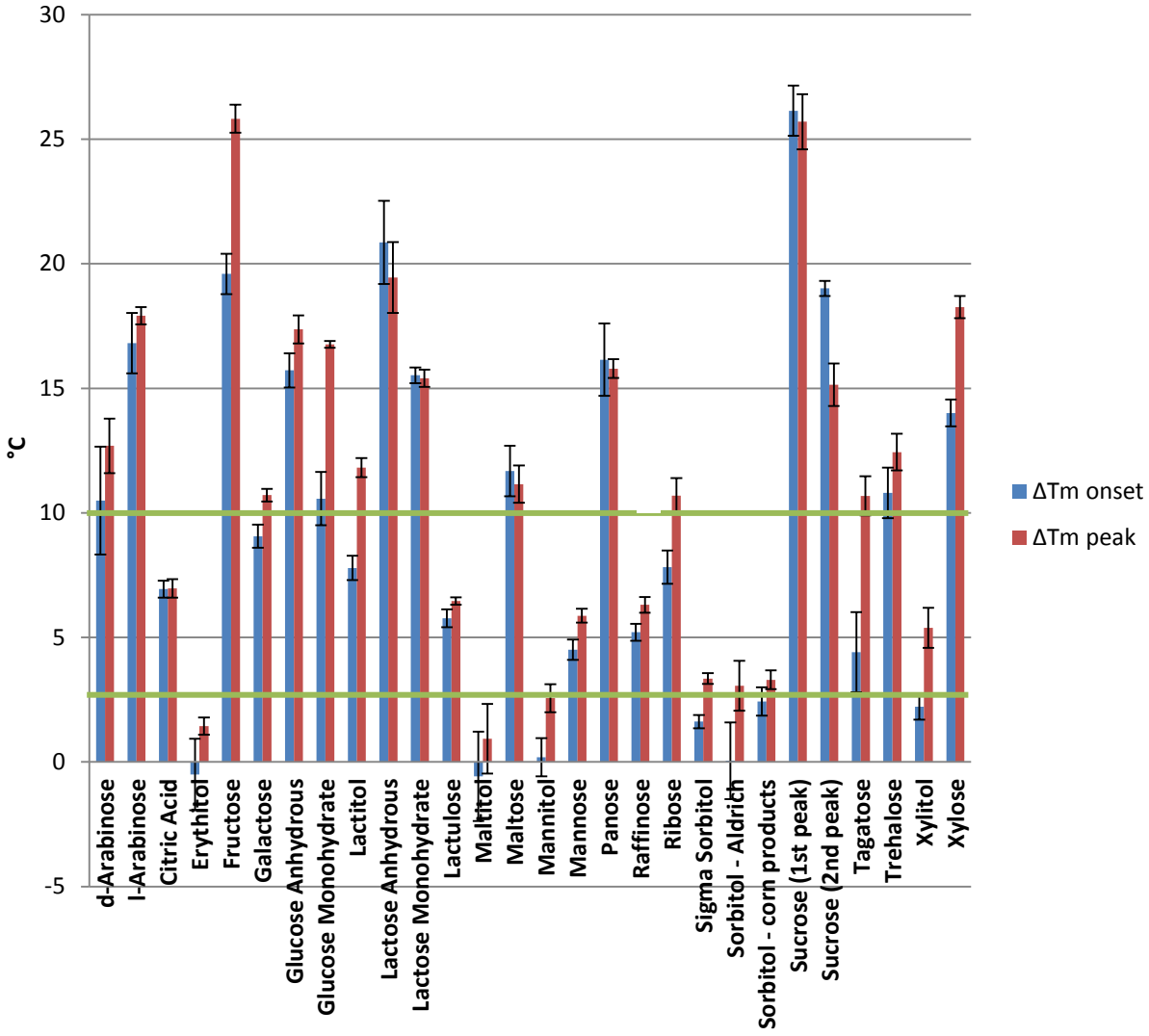

Figure 3-5: Average values of change in onset and peak melting temperature when measured at a rate of 1°C/min and 25°C/min

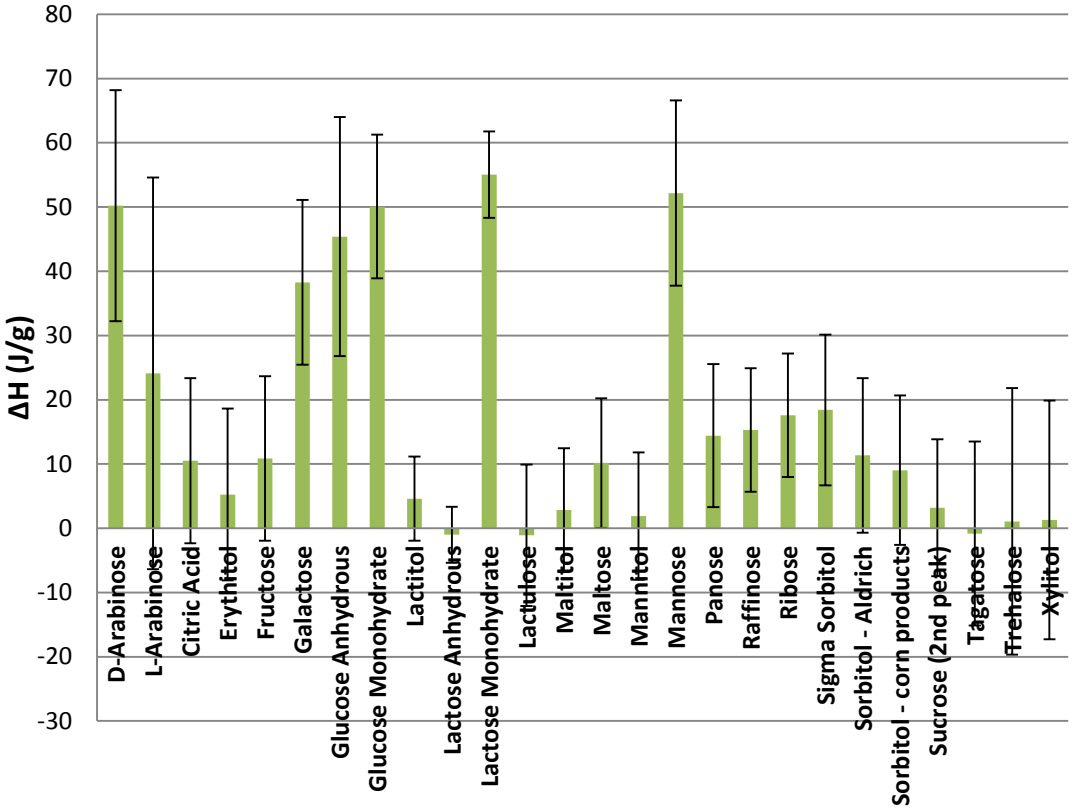

Figure 3-6: Average change in enthalpy between endotherm peaks obtained at a rate of 1°C/min and 25°C/min

Table 3-1: Source, analytical measurements of compounds used in heat rate dependence analysis

Material Name	Type	Source	Lot #	Subgroup in Brand	Purity	C.A.S. #	Ash %	Moisture (as is) %
D-Arabinose	Pentose	Sigma-Aldrich	110K14401	SigmaUltra	99.0%	28697-53-2	<0.05	0.073
L-Arabinose	Pentose	Sigma-Aldrich	BCBB2125V	SigmaUltra	99.0%	5328-37-0	<0.05	0.081
Citric Acid	Acid	Sigma-Aldrich	016M0033V		99.0%	77-92-9	<0.05	0.310
Erythritol	Polyol	Jungbunzlauer	5009299		99.0%	149-32-6	<0.05	0.184
Fructose	Hexose	Sigma	125K01611	SigmaUltra	99.0%	57-48-7	<0.05	0.059
D-(+)-Galactose	Hexose	Sigma-Aldrich	060M0064V		99.0%	59-23-4	<0.05	0.054
Glucose anhydrous	Hexose	Sigma-Aldrich			99.0%	50-99-7	<0.05	0.032
Glucose monohydrate	Hexose	DIFCO	1100002	ACS reagent	99.0%	14431-43-7	<0.05	4.76
Lactitol	Polyol	Xyrofin Oy	21921		99.0%	585-86-4	<0.05	4.94
Lactose anhydrous	Disaccharide	Sigma-Aldrich	BCBD5377	Fluka Analytical	99.0%	63-42-3	0.03	0.435
D-Lactose monohydrate	Disaccharide	Sigma-Aldrich	BCBC1834	Fluka Analytical	99.0%	64044-51-5	0.02	5.013
Lactulose	Disaccharide	Sigma	125F-0623		90.0%	4618-18-2	<0.05	0.081
Maltitol	Polyol	Sigma			99.0%	585-88-6	0.02	0.268
Maltose	Disaccharide	Sigma	58H0881		99.0%	6363-53-7	<0.05	5.150
D-Mannitol	Polyol	Sigma	67H10402	SigmaUltra	98.0%	69-65-8	<0.05	0.065
D-(+)-Mannose	Disaccharide	Sigma-Aldrich	BCBB1636	Sigma Life Science	99.5%	3458-28-4	<0.05	0.034
Panose	Tri-saccharide	Sigma	058H0856		98.0%	33401-87-5	<0.05	0.142
D(+)Raffinose	Tri-saccharide	Sigma-Aldrich	LA44227	Supelco Analytical	99.0%	17629-30-0	Not measured	Not measured
Ribose	Hexose	Sigma	051M182V	SigmaUltra	99.0%	50-69-1	<0.05	0.115
Sorbitol	Polyol	Aldrich	MKBC8755		99.0%	50-70-4	<0.05	0.265
Sorbitol	Polyol	Corn Products			99.0%	50-70-4	<0.05	0.124
Sorbitol	Polyol	Sigma			99.0%	50-70-4	<0.05	0.251
Sucrose	Disaccharide	Sigma Aldrich	090M02112V		99.5%	57-50-1	<0.05	0.028
Tagatose	Hexose	Arla Foods	32404		95.0%	9005-80-5	<0.05	0.091
Trehalose	Disaccharide	Cargill Incorporated	0F021		90.0%	6138-23-4	<0.05	9.812
Xylitol	Polyol	Spectrum	VM0313		99.0%	87-99-0	<0.05	0.168
Xylose	Pentose	Sigma	071k00741	SigmaUltra	99.0%	58-86.6	<0.05	0.037

Table 3-2: Composition and literature reported melting temperature of various compounds organized by molecular weight used heat rate dependence analysis

Material	Formula	Molecular Weight	Method Used	Tm onset °C	Tm peak °C	Enthalpy J/g	Source
D-Arabinose	$C_5H_{10}O_5$	150.1	Not stated	88-92			CRC (2002)
D-Arabinose			DSC rate 5°C/min	150	160	238 J/g	Roos (1993)
D-Arabinose			DSC 10°C/min	153			Slade and Levine (1991)
D-Arabinose			Heat flow calorimeter 1°C/min	135	155	260	Raemy and Schweizer (1983)
L-Arabinose							
Citric Acid	$C_6H_8O_7$	192.124	Not stated	153 anhydrous			Sigma Aldrich , CRC
Erythitol	$C_4H_{10}O_4$	122.1	Not stated	118-120			Sigma Aldrich , CRC
Erythitol			DSC 1°K/min	117.75		240.8 J/g	Barone et al. (1990)
Erythitol			Radiation Calorimeter rate not stated	118.45		342.3 J/g	Spaght et al. (1931)
Fructose	$C_6H_{12}O_6$	180.2	Not stated	119-122			Sigma Aldrich
Fructose			DSC rate 5°C/min	108	127	169 J/g	Roos (1993)
Fructose			Heat flow calorimeter 1°C/min	80	115	180 J/g	Raemy and Schweizer (1983)
Fructose			DSC 10°C/min	124			Slade and Levine (1991)
Galactose	$C_6H_{12}O6$	180.2	Not stated	168-170			Sigma Aldrich
Galactose			DSC rate 5°C/min	163	170	243 J/g	Roos (1993)
Galactose			Heat flow calorimeter 1°C/min	140	165	280 J/g	Raemy and Schweizer (1983)
Galactose			DSC 10°C/min	170			Slade and Levine (1991)
Glucose Anhydrous	$C_6H_{12}O_6$	180.2	DSC 10°C/min	158			Slade and Levine (1991)
Glucose Anhydrous			DSC rate 5°C/min	143	158	179 J/g	Roos (1993)
Glucose Anhydrous			Heat flow calorimeter 1°C/min	200	230		Raemy and Schweizer (1983)
Glucose Monohydrate	$C_6H_{12}O_6$	198.17	Heat flow calorimeter 1°C/min	185	230		Raemy and Schweizer (1983)
Lactitol monohydrate	$C_{12}H_{24}O_{11}$ (Galactose and glucose)	362.33	Not stated	95-98			Sigma Aldrich
Lactose Anhydrous	$C_{12}H_{22}O_{11}$	202.80	Heat flow calorimeter 1°C/min	220	236	700	Raemy and Schweizer (1983)

Table 3-2 (cont.)

α-Lactose Monohydrate	$C_{12}H_{22}O_{11}$		DSC rate 5°C/min		214		Roos (1993)
α-Lactose Monohydrate			Heat flow calorimeter 1°C/min	160	195		Raemy and Schweizer (1983)
Lactulose	C12H22O11 (fructose and galactose)	342.3	Not stated	~169 (decomposes)			Merk Index
Lactulose	C12H22O11		Heat flow calorimeter 1°C/min	130	155	110	Raemy and Schweizer (1983)
Maltitol	C12H24O11 (maltose)	344.31					
Maltitol			DSC rate 5°C/min	139	149	147 J/g	Roos (1993)
Maltitol			Heat flow calorimeter 1°C/min	115	150	150 J/g	Raemy and Schweizer (1983)
Maltose	C12H22O11 (two glucose)	342.3	DSC rate 5°C/min	104 (monohydrate)	123	126 J/g	Roos (1993)
Maltose		342.3	DSC 10°C/min	129 (anhydrous)			Slade and Levine (1991)
Maltose monohydrate			Not stated	102-103			CRC (2002)
Mannitol	C6H14O6 (from Fructose)	182.2	Not stated	167-170			Sigma Aldrich
Mannitol			DSC 1°K/min	165.95		307.9 J/g	Barone et al. (1990)
Mannose	$C_6H_{12}O_6$	180.16	DSC rate 5°C/min	120	134	134 J/g	Roos (1993)
Mannose			DSC 10°C/min	139.5			Slade and Levine (1991)
Panose	C18H32O16	504.5		223			CRC (2002)
Raffinose	C18H32O16 (Galactose,	504.5	Not stated	78-80			Sigma Aldrich
Ribose	C5H10O5	150.1	Not stated	88-92			Sigma Aldrich
Ribose			DSC rate 5°C/min	70	86	146 J/g	Roos (1993)
Ribose			Heat flow calorimeter 1°C/min	60	90	150 J/g	Raemy and Schweizer (1983)
Ribose			DSC 10°C/min	87			Slade and Levine (1991)
Sorbitol	C6H14O6	182.2	Not stated	98-100			Sigma
Sorbitol			DSC 1°K/min	93.35		165.8 J/g	Barone et al. (1990)
Sorbitol				94.35 (B) 88.15 (A)		172.9 (B) 188.2 (A) 188.2 (Γ)	Quinquenet et al. (1988)
Sorbitol			DSC 10°C/min	111			Slade and Levine (1991)

Table 3-2 (cont.)

Sucrose	C12H22O11	342.3	Not stated	189-191			Sigma Aldrich
Sucrose			DSC rate 5°C/min	173	190	118 J/g	Roos (1993)
Sucrose			Heat flow calorimeter 1°C/min	160	185	120 J/g	Raemy and Schweizer (1983)
Sucrose			DSC 10°C/min	192			Slade and Levine (1991)
Tagatose	C6H12O6	180.2	Not stated	133-135			Sigma Aldrich
Trehalose	C12H22O11 (two						
Trehalose			DSC rate 5°C/min	91 (dihydra	97	127 J/g	Roos (1993)
Trehalose		342.3	DSC 10°C/min	203			Slade and Levine (1991)
Trehalose anhydrous			Dynamic Thermal Analysis (DTA) rate not stated	215C			Shafizadeh and Lai (1973)
Xylitol	C5H12O5	152.15	DSC 1°K/min	92.55		245.8 J/g	Barone et al. (1990)
Xylitol			DSC rate 5°C/min	89	95	226 J/g	Roos (1993)
Xylitol			Heat flow calorimeter 1°C/min	65	100	250 J/g	Raemy and Schweizer (1983)
Xylitol			DSC 10°C/min	94			Slade and Levine (1991)
Xylose	C5H10O5	150.1	Not stated	154-158			Sigma Aldrich
Xylose			DSC rate 5°C/min	143	157	211 J/g	Roos (1993)
Xylose			Heat Flow Calorimetery 1°C/min	135	150	280 J/g	Raemy and Schweizer (1983)
Xylose			DSC 10°C/min	153			Slade and Levine (1991)

Table 3-3: Summary of SDSC results, Tm onset (°C), Tm peak (°C) and ΔH (enthalpy) J/g

		1 °C /min			5°C/min			25°C/min		
		onset	peak	ΔH	onset	peak	ΔH	Onset	peak	ΔH
(d) Arabinose	Average	153.62	155.43	216.5	156.32	159.53	217.67	164.11	168.12	266.73
	SD	1.25	0.58	4.38	1.72	1.29	18.66	1.77	0.93	17.44
(l) Arabinose	Average	150.06	151.66	207.51	157.32	158.97	239.49	166.87	169.6	245.69
	SD	0.37	0.07	20.44	0.80	1.46	13.77	1.15	0.34	22.62
Citric Acid	Average	147.79	150.54	225.30	151.75	154.30	201.38	154.89	158.00	235.80
	SD	0.11	0.20	4.34	0.37	0.38	17.42	0.32	0.31	12.10
Erythitol	Average	117.41	119.91	339.88	117.51	119.26	340.80	116.91	121.35	345.12
	SD	1.04	0.20	9.97	0.51	0.13	10.60	0.99	0.28	8.92
Fructose	Average	104.98	112.42	157.84	114.28	121.13	161.77	124.57	138.25	168.71
	SD	0.33	0.07	1.5	0.50	0.15	3.32	0.74	0.56	30.26
Galactose	Average	164.62	167.15	267.69	168.29	171.56	262.32	173.69	177.87	305.96
	SD	0.46	0.25	9.18	0.86	0.33	4.08	0.05	0.01	8.94
Glucose Anhydrous	Average	149.33	152.37	155.47	156.38	159.88	195.58	165.11	169.73	200.87
	SD	0.68	0.55	16.06	0.06	0.17	11.28	0.12	0.11	9.38
Glucose Monohydrate	Average	147.32	150.99	151.86	155.11	158.50	195.21	157.89	167.75	201.93
	SD	0.05	0.03	10.34	0.53	0.25	8.34	1.07	0.13	4.25
Lactitol Monohydrate	Average	92.13	95.29	137.41	94.88	99.63	141.58	99.91	107.10	142.02
	SD	0.13	0.05	4.51	0.12	0.61	4.43	0.47	0.38	4.78
Lactose Anhydrous	Average	211.64	215.56	186.64	225.89	228.67	148.59	232.50	235.01	142.54
(first peak)	SD	0.48	0.38	1.64	0.34	0.38	25.88	1.60	1.37	4.05
Lactose Monohydrate	Average	132.66	133.67	54.76				148.18	149.07	109.81
	SD	0.31	0.26	2.47				0.05	0.23	6.25
Lactulose	Average	160.69	162.81	129.40	166.45	169.27	130.57	164.83	171.18	127.58
	SD	0.24	0.13	4.30	0.24	0.02	3.93	0.27	0.07	10.12
Maltitol	Average	147.11	148.59	162.71	148.45	149.73	169.70	146.52	149.52	165.54
	SD	1.19	1.16	5.82	0.48	0.72	2.54	1.34	0.78	7.67
Maltose	Average	118.49	122.12	146.77	124.25	126.93	149.64	130.16	133.27	156.91
	SD	0.89	0.65	7.93	1.37	0.61	2.14	0.49	0.37	6.25
Mannitol	Average	165.11	166.08	257.11	163.94	166.34	260.38	165.29	168.64	309.28
	SD	0.16	0.07	3.67	0.21	0.06	1.83	0.75	0.56	9.22
Mannose	Average	126.59	129.11	139.03	127.95	131.07	151.54	131.09	134.99	154.18
		0.07	0.22	2.69	0.33	0.23	9.66	0.40	0.17	14.17

Table 3-3 (cont.)

Panose	**Average**	**214.85**	**218.62**	**125.57**	**223.54**	**227.42**	**126.33**	**231.41**	**234.73**	**114.41**
	SD	**1.39**	**0.17**	**9.56**	**0.91**	**0.43**	**4.92**	**0.42**	**0.34**	**15.52**
Raffinose	**Average**	**77.25**	**78.31**	**131.16**	**78.51**	**80.14**	**134.99**	**82.46**	**84.62**	**145.58**
	SD	**0.11**	**0.07**	**7.28**	**0.16**	**0.19**	**13.45**	**0.32**	**0.31**	**6.30**
Ribose	**Average**	**82.15**	**86.52**	**152.58**	**84.26**	**90.45**	**172.03**	**89.97**	**97.21**	**167.87**
	SD	**0.58**	**0.10**	**4.79**	**1.02**	**0.73**	**4.71**	**0.34**	**0.70**	**8.34**
Sigma Sorbitol	**Average**	**93.58**	**96.81**	**147.07**	**93.95**	**97.34**	**162.94**	**95.20**	**100.16**	**164.64**
	SD	**0.12**	**0.01**	**3.61**	**0.32**	**0.37**	**9.22**	**0.24**	**0.22**	**11.17**
Sorbitol - Aldrich	**Average**	**95.32**	**97.37**	**137.97**	**94.27**	**97.59**	**153.27**	**95.37**	**100.42**	**156.38**
	SD	**1.50**	**0.83**	**10.18**	**0.32**	**0.23**	**2.50**	**0.35**	**0.57**	**6.43**
Sorbitol - corn products	**Average**	**94.49**	**96.93**	**142.87**	**95.00**	**97.64**	**163.11**	**96.92**	**100.23**	**154.21**
	SD	**0.24**	**0.07**	**4.67**	**0.49**	**0.57**	**17.29**	**0.52**	**0.37**	**10.66**
Sucrose (1st peak)	**Average**	**133.82**	**139.24**	**0.53**	**147.21**	**153.28**	**0.53**	**159.97**	**164.94**	**1.93**
	SD	**0.87**	**1.01**	**0.13**	**0.35**	**0.34**	**0.12**	**0.51**	**0.45**	**0.43**
Sucrose (2nd peak)	**Average**	**171.34**	**178.88**	**127.42**	**186.66**	**191.11**	**121.04**	**190.44**	**194.03**	**130.63**
	SD	**3.12**	**1.41**	**8.39**	**5.76**	**0.94**	**8.94**	**0.56**	**0.09**	**6.57**
Tagatose	**Average**	**127.00**	**131.64**	**185.48**	**124.95**	**133.87**	**228.27**	**131.41**	**142.32**	**184.66**
	SD	**1.21**	**0.57**	**11.93**	**0.39**	**0.27**	**5.14**	**1.06**	**0.54**	**7.89**
Trehalose	**Average**	**87.56**	**89.62**	**148.32**	**93.79**	**96.32**	**121.40**	**98.35**	**102.06**	**149.38**
	SD	**0.80**	**0.37**	**20.36**	**0.88**	**2.68**	**19.7**	**0.15**	**0.56**	**3.98**
Xylitol	**Average**	**91.49**	**93.06**	**227.08**				**94.27**	**99.38**	**228.38**
	SD	**0.20**	**0.09**	**14.57**				**0.48**	**0.80**	**11.51**
Xylose	**Average**	**141.23**	**145.91**	**204.26**	**147.96**	**153.54**	**213.51**	**155.24**	**164.17**	**227.57**
	SD	**0.36**	**0.29**	**6.85**	**0.34**	**0.13**	**17.14**	**0.40**	**0.34**	**15.72**

Table 3-4: Comparison of reported literature values for Tm onset to values reported in this study.

Material	Lit Values °C	Tested Values °C
D-Arabinose	135-153	153-164
L-Arabinose	135-153	150-167
Citric Acid	153	147-155
Erythitol	117-122	117
Fructose	80-124	105-124
Galactose	140-170	164-174
Glucose Anhydrous	143-200	149-165
Glucose Monohydrate	185	147-158
Lactitol Monohydrate	95-98	92-99
Lactose Anhydrous	214-220	211-230
Lactose Monohydrate	160	132-148
Lactulose	130	160-164
Maltitol	115-139	146-147
Maltose monohydrate	102-104	118-130
Mannitol	166-170	165
Mannose	120-140	126-131
Panose	223	215-231
Raffinose	78-82	77-82
Ribose	60-92	82-90
Sorbitol	88-111	93-97
Sucrose (1st peak)	160-192	161-163
Sucrose (2nd peak)	160-192	166-187
Tagatose	133-135	127-131
Trehalose	91	87-98
Xylitol	65-95	91-94
Xylose	135-158	141-155

Table 3-5: Difference between 1°C/min and 25°C/min $\Delta T_{m\ onset}$ (°C) and $\Delta T_{m\ peak}$ (°C)

Material	$\Delta T_{m\ onset}$	Standard deviation	$\Delta T_{m\ peak}$	Standard deviation
D-Arabinose	10.49	2.17	12.69	1.10
L-Arabinose	16.81	1.21	17.94	0.35
Citric Acid	6.94	0.34	6.97	0.37
Erythitol	-0.50	1.44	1.44	0.34
Fructose	19.59	0.81	25.82	0.56
Galactose	9.06	0.46	10.71	0.25
Glucose Anhydrous	15.72	0.69	17.36	0.56
Glucose Monohydrate	10.57	1.07	16.76	0.13
Lactitol	7.79	0.49	11.81	0.38
Lactose Anhydrous	20.86	1.67	19.44	1.42
Lactose Monohydrate	15.52	0.31	15.40	0.35
Lactulose	5.77	0.36	6.46	0.15
Maltitol	-0.58	1.79	0.93	1.40
Maltose	11.68	1.02	11.15	0.75
Mannitol	0.19	0.77	2.56	16.36
Mannose	4.51	0.41	5.87	0.28
Panose	16.15	1.45	15.79	0.38
Raffinose	5.21	0.34	6.31	0.32
Ribose	7.82	0.67	10.69	0.71
Sigma Sorbitol	1.62	0.27	3.35	0.22
Sorbitol - Aldrich	0.05	1.54	3.06	1.01
Sorbitol - corn products	2.43	0.57	3.30	0.38
Sucrose (1^{st} peak)	26.14	1.01	25.70	1.11
Sucrose (2^{nd} peak)	19.01	0.30	15.14	0.85
Tagatose	4.41	1.61	10.68	0.79
Trehalose	10.80	1.01	12.44	0.74
Xylitol	2.22	0.52	5.39	0.81
Xylose	14.01	0.54	18.26	0.45

Table 3-6: Classification of screened compounds into No/Low, Medium or High change of $\Delta T_{m\ onset}$ (°C) depending on heating rate

No/Low Heat Rate Dependent <2°C	Medium Heat Rate Dependent 2 to 10 °C	High Heat Rate Dependent >10°C
Erythitol	Citric Acid	D-Arabinose
Maltitol	Galactose	L-Arabinose
Mannitol	Lactitol	Fructose
Sorbitol[a]	Lactulose	Glucose Anhydrous
Xylitol	Mannose	Glucose Monohydrate
	Raffinose	Lactose Anhydrous
	Ribose	Lactose Monohydrate
	Tagatose	Maltose
		Sucrose
		Trehalose
		Xylose

[a] Repeatable from three sources.

Table 3-7: Comparison of Enthalpy Data from DSC at 1°C/min and 25°C/min and the difference between the two rates

Material	H at 1°C/min	H at 25°C/min	ΔH (J/g)	ΔH Standard Deviation
D-Arabinose	216.54	266.73	50.20	17.98
L-Arabinose	221.58	245.69	24.11	30.49
Citric Acid	225.30	235.8	10.50	12.85
Erythitol	339.88	345.12	5.24	13.38
Fructose	157.84	168.71	10.87	12.80
Galactose	267.69	305.96	38.27	12.81
Glucose Anhydrous	155.47	200.87	45.40	18.60
Glucose Monohydrate	151.86	201.93	50.07	11.18
Lactitol	137.41	142.02	4.61	6.51
Lactose Anhydrous	186.6	142.5	-1.10	4.36
Lactose Monohydrate	54.76	109.81	55.05	6.72
Lactulose	129.40	114.58	-1.08	10.99
Maltitol	162.71	165.54	2.83	9.63
Maltose	146.77	156.91	10.14	10.09
Mannitol	257.11	259.00	1.89	9.92
Mannose	139.03	154.18	52.17	14.42
Panose	131.16	145.58	14.42	11.12
Raffinose	152.58	167.87	15.29	9.63
Ribose	147.07	164.64	17.57	9.62
Sigma Sorbitol	137.97	156.38	18.41	11.74
Sorbitol - Aldrich	142.87	154.21	11.34	12.04
Sorbitol - corn products	126.96	136.00	9.04	11.63
Sucrose (2nd peak)	127.42	121.04	3.21	10.66
Tagatose	185.48	184.66	-0.83	14.30
Trehalose	148.32	149.38	1.06	20.74
Xylitol	227.08	228.38	1.30	18.57
Xylose	204.26	227.57	23.31	17.14

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CHAPTER 4

Thermal Analysis Characterization of the Loss of Crystal Structure in Select Monosaccharides, Xylitol and Citric Acid

Abstract

L- and D- arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, ribose, xylose, xylitol and citric acid were tested to understand their thermal behavior using regular MDSC, quasi-isothermal MDSC and TGA. Using regular MSDC did not yield any meaningful signals outside of total heat flow. The equations used to calculate the regular MDSC signals could not be applied during the loss in crystal structure event, since the modulated heating rate cannot be controlled during the loss of crystal structure. The quasi-isothermal MDSC yielded important information in regards to the reversing heat capacity (Cp) signal. If the reversing Cp signal exhibited signs of recrystallization during melting and returned to the baseline at the end of the heating process, the material exhibited thermodynamic melting. If it did not, the material was classified as apparent melting. An overlay of plots for Tm onset from DSC and Ti (onset of initial decomposition) from TGA showed that three compounds (L- arabinose, D- arabinose and galactose) exhibited a loss in weight that occurred before the onset of the loss in crystalline structure, even without taking thermal lag into consideration. Glucose monohydrate exhibited that weight loss occurs substantially before the onset of the loss of crystalline structure, but the early weight loss is attributed to the loss in hydrate water. Fructose loss of crystalline structure and onset of decomposition overlay showed both events occurring at a similar temperature. Xylose and ribose overlay weight loss occurred at a time slightly after the onset of the loss of crystalline structure. The onset of decomposition occurred significantly after the loss of crystalline structure in xylitol. The citric acid Tm onset occurred before the Ti. The difference between Tm onset from DSC and the Ti from TGA were similar numerically for the sugars and citric acid (<15°C), but very different for the polyol (~125°C). Through comparison of Tm onset to Ti and through reversing Cp results from Quasi-isothermal MDSC, L- and D- arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, ribose, and xylose were found to be apparent melting materials, whereas xylitol was found to be a thermodynamic melting material. The results on citric acid were inconclusive.

Introduction

Screening of 25 carbohydrate type compounds in Chapter 3 revealed three heating rate dependent behavior groups: no/low, medium, high. It is necessary to begin to explore the heating behavior in each of the three groups (no/low heating rate dependent, medium heating rate dependent, and high heating rate dependent). The purpose of this research is to identify tools to further classify compounds as thermodynamic or apparent melting materials. Typically, decomposition can be proven by the identification of degradation compounds (Maga, 1989). Decomposition compounds can be detected using HPLC, but the decomposition pathway must be known in order to identify the correct initial decomposition compounds. These limitations make it difficult and time-consuming to identify if decomposition is occurring by HPLC identification of decomposition compounds. A search of the literature suggests other methods that may indicate the thermal behavior of compounds as they proceed through the melting process.

Modulated DSC is a method used to give additional information about the thermal behavior of compounds (Thomas, 2001). The total heat flow measured by modulated DSC can be separated into two components, reversing and non-reversing heat flow. The reversing heat flow is generally caused by heat capacity and changes in heat capacity such as glass transitions and loss of crystal structure. The reversing fraction is called the heat capacity component (also termed the reversing heat flow) and is shown as the reversing heat flow signal in a MDSC thermogram. The non-reversing heat flow can be calculated by subtracting the reversing heat flow from the total heat flow. The non-reversing fraction is caused by kinetic processes, such as decomposition, evaporation, chemical reactions, and crystallization. The non-reversing fraction is called the kinetic component (also termed the non-reversing heat flow) and is shown as the non-reversing heat flow signal in a MDSC thermogram (Thomas, 2006). Modulated DSC will give information on the types of events occurring during the heating of the materials. The modulation and equations used in MDSC give information on whether the events are thermodynamic or kinetic in nature.

The second method used, called stepwise quasi-isothermal MSDC, involves a small temperature modulation which is applied to a constant average temperature for a relatively long period of time. Changes in heat capacity indicate a change in structure caused by a thermal event. A kinetic event or process can be observed by measuring a change in Cp. Table 2-15 lists the signals used in quasi-isothermal DSC. In quasi-isothermal DSC method, a change in Cp is seen in the reversing Cp signal

because the reversing Cp is associated with the modulated heating rate. In the case of quasi-isothermal DSC, the average heating rate is zero.

Thirdly, TGA is used to understand the application of heat and the resulting loss of weight in the material. A thermogram from the TGA can provide several characteristics, including weight loss and the derivative weight loss (%/C). Plotting weight loss versus temperature will show the temperature at which initial weight loss occurs (indicating decomposition temperature). In carbohydrates, decomposition eventually results in weight loss, though in many carbohydrates (e.g. sucrose) weight loss does not occur in the first step in decomposition. In monosaccharides, the first steps of decomposition are the triple dehydration of the monosaccharide resulting in HMF or furfural formation (HMF for hexoses, and furfural for pentoses)(Lewkowski, 2001). Though even in the case of monosaccharides the temperature must be over 100°C for there to be a loss in weight, the temperature must be high enough to evaporate the water molecule formed during decomposition. Understanding the decomposition pathway will help interpret the temperature of initial weight loss given from the TGA and how it is related to the temperature of initial decomposition.

A derivative temperature plot (°C/min) from the TGA can monitor the heating rate of a material during a phase transition, such as the loss of crystalline structure. During a phase change for the carbohydrates (in this case, loss in crystal structure), energy applied affects the phase transition (latent heat) and is not available to raise the temperature of the material. When the compound is not undergoing a phase transition, heat would be applied resulting in a temperature increase (sensible heat). Therefore, monitoring the heating rate will determine if a sample is using latent heat or sensible heat, and comparing the onset of the phase transition can correspond to the onset of loss in crystal structure. TGA is a method used to evaluate the stability of compounds by measuring the weight of a compound during controlled experiments. These can be oxidative or thermal processes. In this case, if a product goes through decomposition around or before the Tm onset determined by DSC, it should be seen in the TGA by a corresponding loss of weight (if weight loss is part of the thermal decomposition event). In sugars there is a loss in weight as decomposition proceeds.

When analyzing the DSC curves obtained in the screening of compounds in Chapter 3, the total heat flow gave a perspective of the thermal behavior of the materials. The challenge is to understand the thermal behavior both in the DSC and the TGA. If decomposition is really occurring and causing a loss in crystalline structure in some sugars as Lee et al. (2011a) assert, then the relation of decomposition in the TGA to heat flow in the DSC can be correlated as soon as the decomposition

results in a loss in weight. Hurtta et al. (2004) and Lappalainen et al. (2006) compared Tm onset as measured in the DSC and Ti (initial decomposition temperature) from the TGA. They concluded that decomposition affects melting. Another of the pitfalls of the comparison is the difference in thermal lag (especially at high heating rates) between the two techniques. In the TGA, the temperature probe is suspended above the sample pan. In the DSC, the temperature probe is touching the bottom of the pan (but not the sample). In both cases there would be a thermal lag, a difference between the measured temperature and the temperature of the sample, but the thermal lag would be greater in the TGA because of the distance between the probe and the sample. Care then needs to be taken when comparing the temperatures of the onset of loss in crystal structure to the temperatures of the onset of decomposition when measured with different techniques.

The objective of this research was to apply the various thermal techniques (MDSC, quasi-isothermal MDSC, and TGA) to gain an understanding of the thermal behavior of several monosaccharides (xylose, fructose, glucose monohydrate, glucose anhydrous, ribose, galactose, and D arabinose, L arabinose) and related carbohydrate compounds (xylitol and citric acid).

Xylose and arabinose are in the high heat rate dependency group and have not previously been investigated for behavior as apparent melting materials. Fructose and glucose were added to this set of experiments to increase the understanding of the thermal behavior of these materials. Lee et al. (2011b) showed heating rate dependent melting behavior for fructose and glucose, and additional experiments will add to our understanding of their thermal behavior. Ribose was added since it is a 5-carbon sugar (pentose) like arabinose and xylose but in the medium heat rate dependence group. Galactose, in the middle change group, will also be further investigated since it is a 6-carbon sugar of biological importance that has not previously been investigated regarding apparent or thermodynamic melting. The sugars are all monosaccharides with a hydroxyl group per carbon and one carbonyl group. Xylitol was selected from the no/low heating rate dependency group to compare to xylose since xylitol is the sugar alcohol corresponding to xylose. Lappalainen et al. (2006) published work using xylitol instead of indium to measure thermal lag in their experiments on L- and D-xyloses. Xylitol was explained to have “normal” melting behavior. Lee et al. (2011b) used mannitol as a comparison material in their work with sucrose because of its predictable thermal behavior. The xylitol molecule contains hydroxyl groups (one per carbon) as the only functional group. Citric acid will be investigated further as a non-sugar carbohydrate type compound. Citric acid is a 6-carbon carboxylic acid containing similar functional groups and number of carbons to the sugars. The citric acid has a carboxylic acid (carbonyl

group and a hydroxyl on the same carbon) as well as hydroxyl groups. This research will explore several rapid screening methods to give information on what is occurring during the heating of select compounds from the three heating rate dependent groups identified in the previous chapter.

Materials and Methods

Materials

The following sugars were selected from previous screening in Chapter 3 for more in-depth testing:

No/Low heat rate dependent group: xylitol

Medium heat rate dependent group: ribose, galactose and citric acid

High heat rate dependent group: xylose, D and L arabinose, fructose and glucose monohydrate and glucose anhydrous

These sugars and related compounds will be analytical grade and obtained from the same suppliers as shown in Table 3-1.

MDSC Method

MDSC was performed in the modulated mode using the Discovery DSC (TA Instruments, New Castle, DE). The instrument was calibrated using a sapphire disk (PN 970370.901, TA Instruments, New Castle, DE). Dry nitrogen purge gas was set at a flow rate of 50 mL/min. MDSC was run in a range through the loss in crystal structure temperatures on the selected compounds; the range and rate were the same as the SDSC experiment in Objective 1 (room temperature to 200°C except for xylitol, which was room temperature to 250°C) at modulation amplitude of ± 1.0^{o}C for 100 seconds.

Stepwise Quasi-isothermal MDSC

Step-wise-isothermal MDSC was performed using the modulated mode on the DSC Q2000. The instrument was calibrated using a sapphire disk (PN 970370.901, TA Instruments, New Castle, DE). Dry nitrogen purge gas was set at a flow rate of 50 mL/min. Stepwise MDSC used a modulated heating rate with a modulation amplitude of ± 1.0^{o}C and a period of 100 sec applied to the sugar for 30 minutes at increasing temperature steps (e.g. 60 to 120°C) across the range of temperatures in which the loss of crystalline structure occurred as determined by SDSC; displayed in Table 4-1. Data was collected after a

five minute data off period for initial equilibration at each temperature. All sample measurements were done in triplicate. Results were displayed as plots of Rev C_p, modulated heat flow, and temperature against isothermal time using the UA software. It is hypothesized that if recrystallization does not take place during the modulation, it could indicate that the compound has chemically changed and cannot recrystallize. Also a permanent substantial change in Cp would indicate a change in chemical composition of the materials.

Thermogravimetric Analyzer (TGA)

For TGA experiments, sugars were heated at heating rates of 1, 5, and 10^{o}C/min over the same temperature range as in the SDSC experiments. The lower heating rate of 10 ^{o}C/min (instead of 25°C/min) was used for the TGA measurements because of the greater thermal lag observed in TGA. The thermal lag was greater in the TGA since the thermocouple was not in contact with the sample pan. Weight loss was plotted as a function of temperature to determine the onset of decomposition. In some sugars, the first step of decomposition may not be a loss in volatiles, but rather a condensation reaction. The onset temperature shown by these experiments was the temperature at which a loss in weight due to volatile production was observed. The beginning of decomposition (condensation reaction) began before the onset temperature, but since there is little to no change in weight, the actual onset temperature of decomposition cannot be detected by TGA method.

Results and Discussion

MDSC Results

The MDSC experiments did not provide meaningful results. At the melting temperature, there is equilibrium between the crystalline and amorphous phases and the sample's temperature remains invariant until the complete loss of crystal structure. Therefore the modulated heating rate cannot be controlled. In apparent melting materials, the situation is even more complicated, since energy is also being employed for the decomposition reactions. In all materials, the energy applied to the sample is being used for the latent heat of fusion, and during the loss in crystal structure there is no change in temperature. The MDSC cannot control the temperature or maintain a heating rate during the temperature range where the loss of crystal structure is taking place. This loss in heating rate control during the melting event can be seen in Figure 4-1. Examining at the derivative heat flow, a nearly flat

line or loss of temperature change (heating rate) in the range of the endothermic loss of crystal structure is revealed. The equation for calculation of the MDSC signals is the Total heat flow = reversing heat flow + non reversing heat flow.

$$\frac{dH}{dt} = Cp\frac{dT}{dt} + \square(\mathrm{T}, \mathrm{t}) \qquad \text{Equation Number 1}$$

Thus, as the slope of the heat flow goes to zero, though the software attempts to, it becomes impossible to calculate the reversing (thermodynamic) and non-reversing (kinetic) components of the total heat flow signal. The result is that the total heat flow is the only signal that can be used from the MDSC results. From total heat flow, Tm onset, Tm peak and H (enthalpy) can be obtained. SDSC also gives these parameters, so using MDSC is not effective. Tm onset for the heating rate of 1°C/min from the MDSC is reported in Table 4-2. These results show the same trends as the SDSC results as can been seen in Table 4-7. As expected, the SDSC results for Tm onset at 1°C/min and the MDSC results for Tm onset at 1°C/min reported in Table 4-7 are very similar. The trend is that the MDSC Tm onset is at a slightly higher temperature, but the slightly higher MDSC temperature is probably attributable to the effect of the modulating temperature employed in the MDSC.

Stepwise Quasi Isothermal Results

Using SDSC results, an appropriate temperature range for each sugar was selected for the stepwise quasi-isothermal experiments. The temperature range used for each sugar is provided in Table 4-1. Stepwise quasi-Isothermal results were shown by Lee et al. (2011a) to be substantially different between sucrose (apparent melting) and mannitol (thermodynamic melting). Lee et al. (2011a) compared the signal for modulated heat flow and reversing heat capacity. When analyzing the mannitol, it was found that during melting, the reversing heat capacity (Cp) changes, but returns to the original baseline value. For sucrose, the reversing heat capacity changed and did not return to the baseline. The onset temperature, the Cp value and temperature when it stabilized, and the difference between the two values were recorded for each sugar. The quasi-isothermal thermogram for fructose is show in Figure 4-2, the onset, and final Cp are marked. Using Figure 4-2 as a guide, results were tabulated for each material and are shown in Table 4-3. Included in the results are the ΔCp and ΔT indicating the amount of difference between the onset and final values.

The values themselves do not illustrate the differences in the materials. Because the two simultaneous endothermic processes (heat capacity and latent heat of fusion) respond differently to

temperature modulation, and because of the difference in activation energy for each of the sugars, the signals become difficult to interpret (Thomas, 2015). The D-arabinose, glucose anhydrous, ribose, xylitol and citric acid all exhibit changes in Cp, which are less than one, and all other materials (L-arabinose, fructose, galactose, glucose monohydrate, xylose and citric acid) have changes in Cp that are greater than one. The difference in temperature (ΔT) between the beginning of the change in Cp to the final leveling off ranges from ΔT=2.33 for galactose to ΔT=14 for citric acid. The essential difference in the stepwise quasi-isothermal results is revealed when observing the shape of the reversing Cp curve. The shapes of the plots of the reversing heat capacity (Cp) are summarized in Table 4-4. The shapes have been given two descriptions: "S-curve" and "up and back". For comparison, the thermograms are available in Figure 4-3 through Figure 4-8. Ultimately, the difference between a reversing heat capacity that returns to close to the original baseline value after the melting event (up and back) and one which permanently changes and does not return to a lower value (S-curve) provides the most important information. These results show that the sugars L- and D- arabinose, fructose, galactose, glucose, and xylose all have a reversing Cp that do not decrease again after the melting event, but remain permanently elevated. Observing the maximums of the modulated heat flow signal exhibit that these sugars do not recrystallize during modulation over the range where loss in crystalline structure is observed. Recrystallization would be seen as increase in the maximums of the modulated heat flow signal during the range of temperature over which a loss in crystalline structure is observed. The loss in crystalline structure can be observed by looking at the minimums in the modulated heat flow signal. The permanent change in Cp indicates that the material has chemically changed and, in turn, the chemical change indicates that apparent melting has occurred. Xylitol did return to values of reversing heat capacity similar to the original value, which indicates no chemical change and that xylitol underwent thermodynamic melting. Citric acid contains a peak in Cp like xylitol, but the final value in Cp is different from the initial value. Citric acid also shows an increase in the maximum values for modulated heat flow, indicating the sample is able to recrystallize. Chemical changes taking place can be verified by identification of the decomposition products or a confirmation of the loss in initial material.

TGA Results

When interpreting the TGA results it is important to remember that the TGA measures the weight of the sample as the temperature changes. After initial water loss, a further loss in weight

demonstrates decomposition, although depending on the pathway, the initial temperature of decomposition may not be shown. Weight loss will only be recorded when decomposition has gone long enough for there to be volatiles formed or at temperatures high enough to allow the decomposition product to be volatilized. For example, galactose showed a high level of products that exhibited weight gain compared to other sugars when heated at 180°C for 2 hours (Golon and Kuhnert, 2013). Golon and Kuhnert (2013) showed 43 decomposition compounds for mannose heated at 180°C for 2 hours, only 8 of which had a lower molecular weight than mannose itself; the lower molecular weight would typical mean the products are more volatile. The main volatiles in the decomposition of sugars are carbon dioxide and water.

To interpret the TGA results, the percent weight loss was plotted as a function of temperature, and a weight loss onset (Ti onset) was calculated using the Universal Analysis software. Results are shown in Table 4-5. The difficulty is that a closer look at the TGA curve indicates the signal actually leaves the baseline (begins to lose weight) before the software calculated onset temperature. In this experiment, the very lowest temperature that we start to record a loss in weight (the very lowest temperature decomposition can be observed to occur) should be compared to the onset of the loss in crystal structure. Because of the slow initial loss in weight observed in the TGA, a second set of data were calculated. The second set of data looks at a loss of 0.1% weight after the initial equilibration of water loss and calculates the onset from the baseline to 0.1% weight loss using the Universal Analysis software. By examining the weight loss at 0.1%, a more accurate onset temperature can be determined. This second set of more sensitive data is shown in Table 4-6. As would be expected in a kinetic event, the decomposition onset temperature is heating-rate dependent. A lower heating rate will result in a lower Ti (onset temperature of decomposition). The results reflected these trends among the sugars and citric acid, but not for xylitol.

Ti measured by TGA (TGA onset measured in the full scale) at 1°C/min is compared in Table 4-7 to the Tm onset as measured by SDSC and MDSC. These Ti onset temperatures occur in the same range as the Tm onset temperatures (difference of <15°C), with the exception of xylitol, which has a Ti that is significantly higher than its Tm onset (Tm onset of 91.49 and 92.17°C and Ti of 216.62°C), which is a difference of 125°C.

An interesting comparison is to overlay the SDSC and TGA data at the same heating rate. The overlay illustrates that for every sample (except for xylitol) decomposition occurs in the same temperature range as the loss in crystalline structure. Most monosaccharides begin decomposition with

the opening of the ring structure, and then the loss of a water molecule (Lewkowski, 2001). Because of the thermal lag between the instruments and initial steps of decomposition not resulting in a loss in weight, a complete correlation may not be possible.

L- Arabinose, D- arabinose, and galactose overlays show decomposition occurring before the onset of loss of crystalline structure (Figure 4-11, Figure 4-12, Figure 4-14). Glucose monohydrate loss of weight occurred significantly before Tm onset, but initial weight loss seen in the TGA is the loss of monohydrate water, not decomposition (Figure 4-16) (Lee et al., 2011a). Glucose anhydrous loss in weight occurs at the same temperature as Tm onset (Figure 4-15). Fructose onset of decomposition and Tm onset overlay show both events happening at a similar temperature. Xylose (Figure 4-18) and ribose (Figure 4-17) overlay show decomposition at a temperature slightly after onset of melting. In the case of ribose, melting occurs below 100°C, and the water produced by decomposition would not be able to leave the sample until 100°C. The thermogram shows the loss in weight around 100°C, so the difference in melting and onset of weight loss is probably explained by the low temperature (lack of volatiles). Xylitol in Figure 4-19 displays the onset of decomposition occurs substantially after melting. In the case of citric acid, the overlay demonstrates that the onset of weight loss in decomposition occurs slightly after the Tm onset (Figure 4-20). All of these results will be affected by thermal lag, but because of the proximity of the temperature probe to the sample, the TGA will exhibit more thermal lag than the DSC. When interpreting events that occur at similar temperatures, thermal lag must be taken into account. Because of thermal lag, events will be shifted to the right (or seem to occur at a higher temperature) with the TGA curve exhibiting more thermal lag than the DSC.

The values obtained for Ti onset in this experiment are compared to the Ti onset from literature in Table 4-8. The values are similar, but there is some variability. The results obtained for Ti onset in this experiment were different depending on the method used for determining the Ti onset. The literature values could also differ depending on the source and purity of the material.

Conclusions

MDSC results beyond Tm onset, Tm peak and total heat flow cannot be used because the modulated heating rate cannot be controlled during loss of crystal structure. The quasi-isothermal MDSC method yielded important information in regards to the reversing heat capacity (Cp) signal. If the reversing Cp signal returned to the baseline at the end of the heating process, as was observed in the case of xylitol, the material exhibited thermodynamic melting. If the reversing Cp did not return to the

baseline, the material was classified as apparent melting. L- and D- arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, ribose, and xylose displayed a reversing Cp signal that did not return to baseline and would therefore be classified as apparent melting materials. The citric acid results were inconclusive and require more investigation. Comparing the Tm onset by DSC and the Ti onset of decomposition by TGA revealed that the sugars and citric acid have onsets in close proximity, <15°C; whereas xylitol onset values are much further apart (approximately 125°C). The comparison of Tm onset to Ti also indicates that L- and D- arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, ribose, and xylose are classified as apparent melting materials, xylitol is a thermodynamic melting material and citric acid is inconclusive. In order to positively prove apparent melting, experiments should be done to identify decomposition products at temperatures below the Tm onset temperature.

Figures and Tables Chapter 4

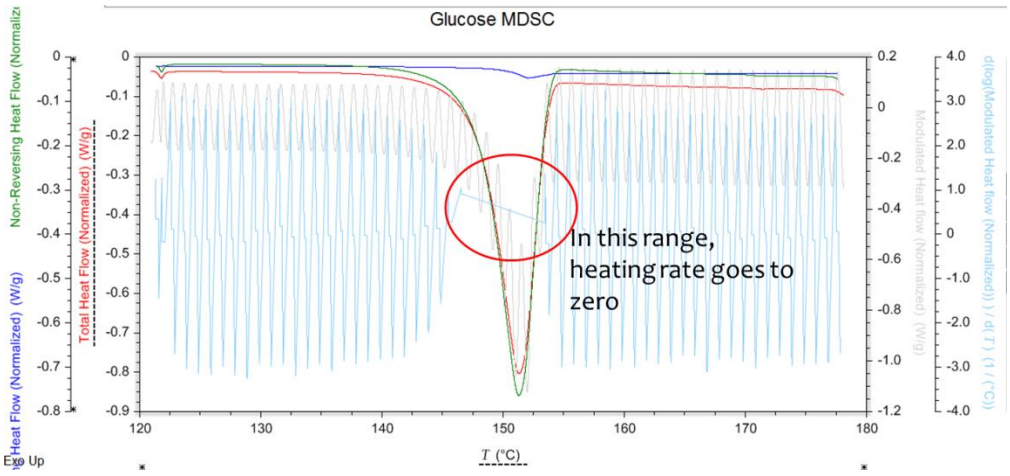

Figure 4-1: Heat flow, reversing and non-reversing, total heat flow, modulated heat flow and the derivative of the modulated heat flow of MDSC of glucose showing the derivative heat flow. The derivative of the heat flow shows the heating rate approaching zero during the melting event

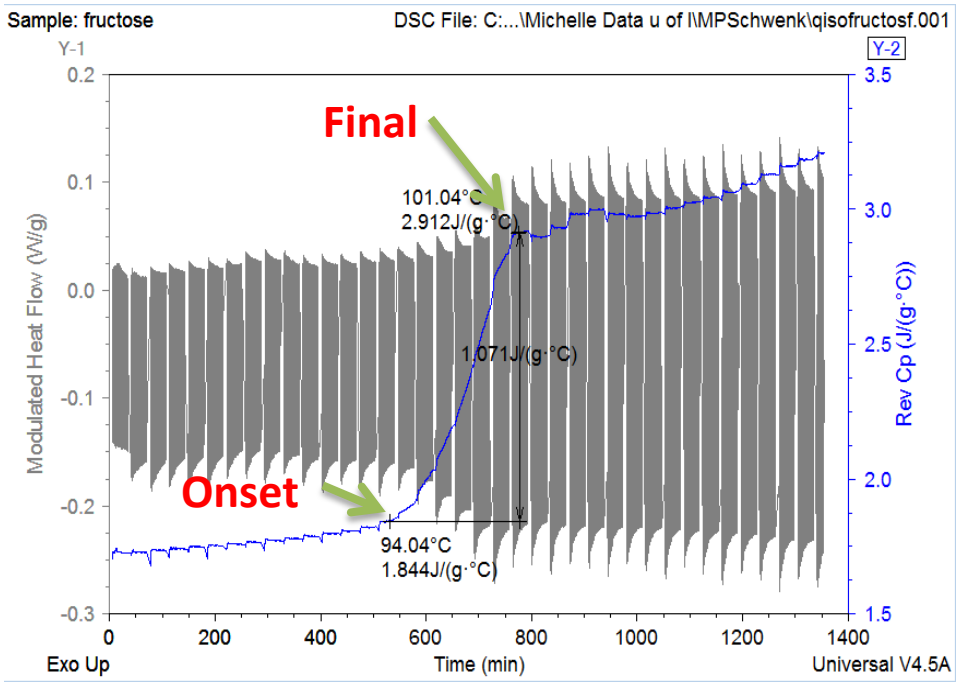

Figure 4-2: Location of Onset Temperature and Cp and Final Temperature and Cp of fructose

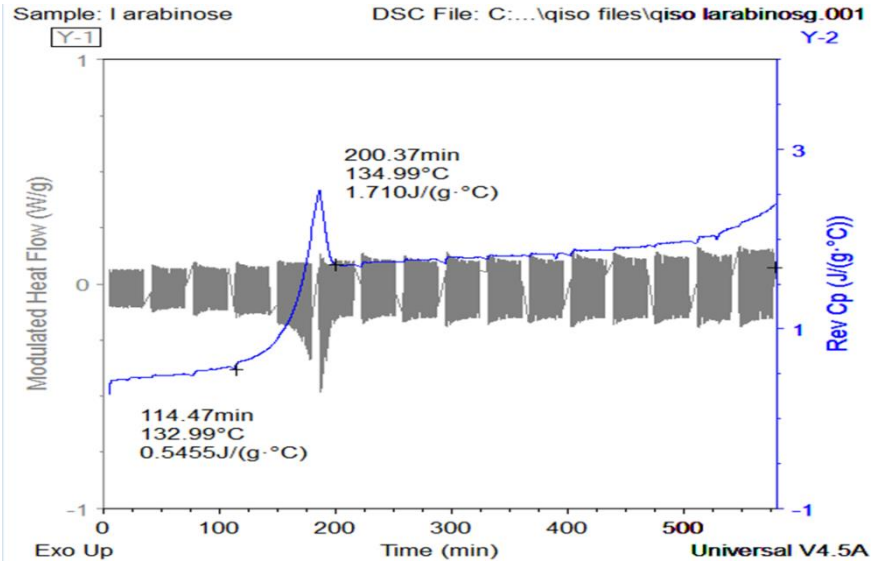

Figure 4-3: Reversing Cp versus time from Quasi-Isothermal experiment for L-arabinose

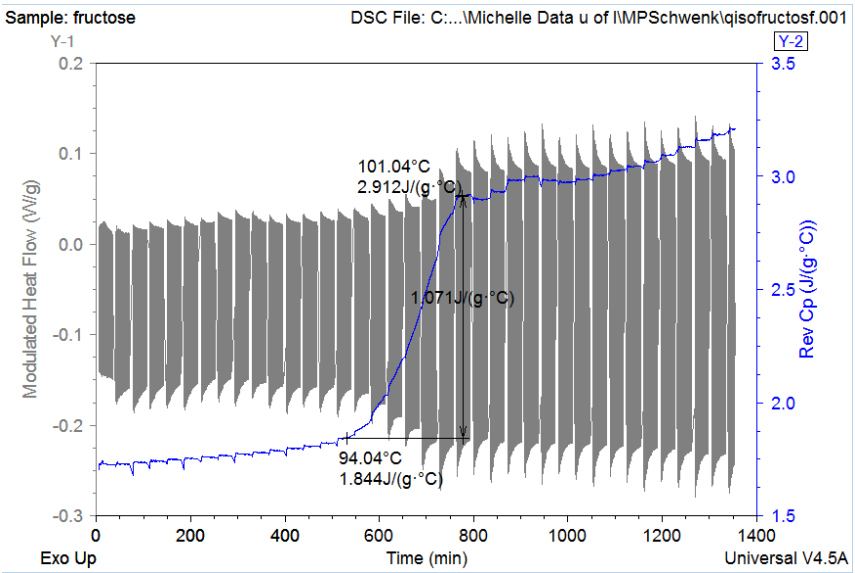

Figure 4-4: Reversing Cp versus time from Quasi-Isothermal experiment for fructose

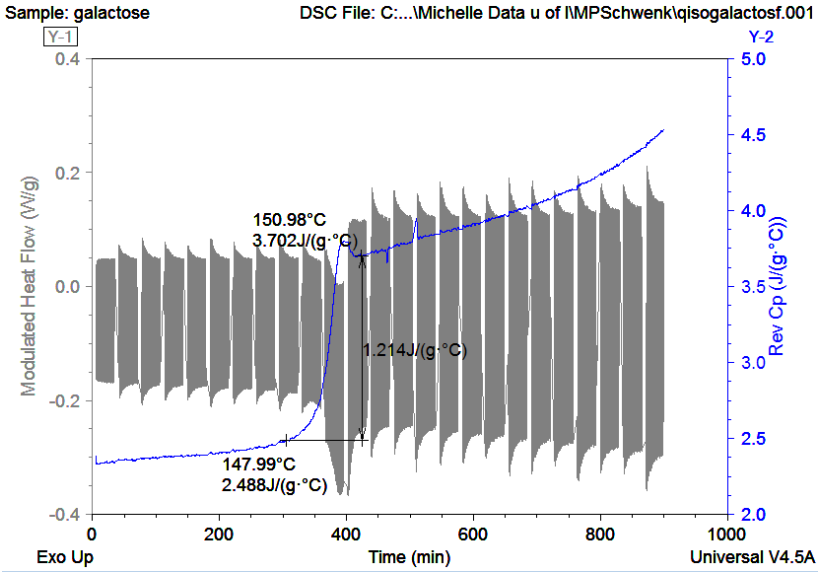

Figure 4-5: Reversing Cp versus time from Quasi-Isothermal experiment for galactose

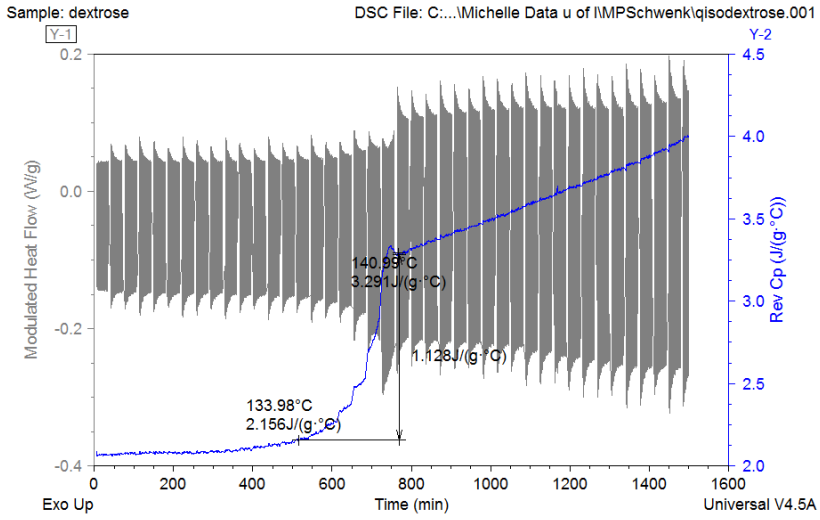

Figure 4-6: Reversing Cp versus time from Quasi-Isothermal experiment for glucose monohydrate

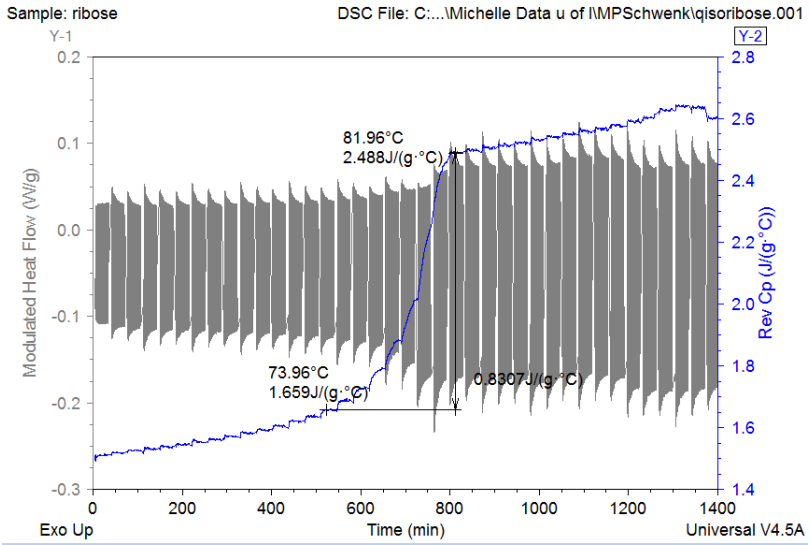

Figure 4-7: Reversing Cp versus time from Quasi-Isothermal experiment for ribose

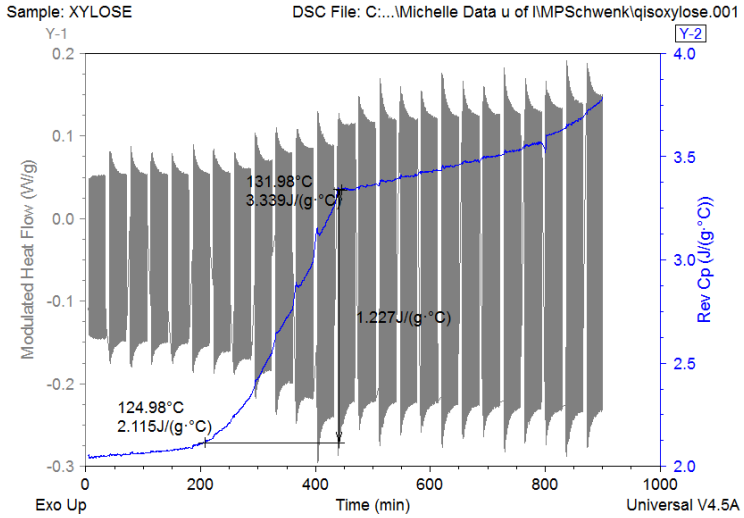

Figure 4-8: Reversing Cp versus time from Quasi-Isothermal experiment for xylose

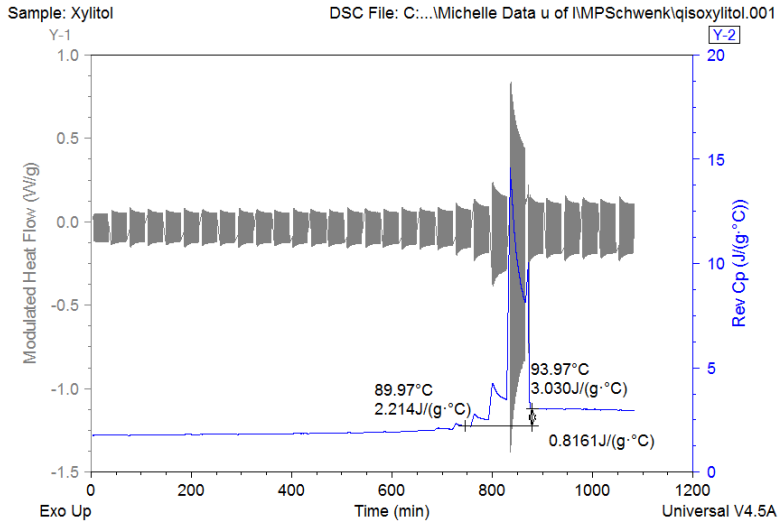

Figure 4-9: Reversing Cp versus time from Quasi-Isothermal experiment for xylitol

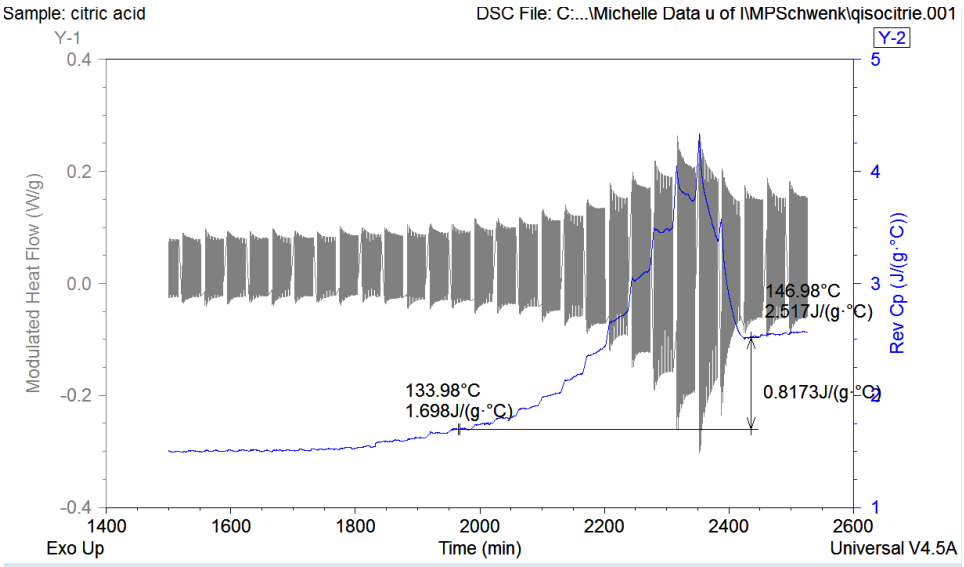

Figure 4-10: Reversing Cp versus time from Quasi-Isothermal experiment for citric acid

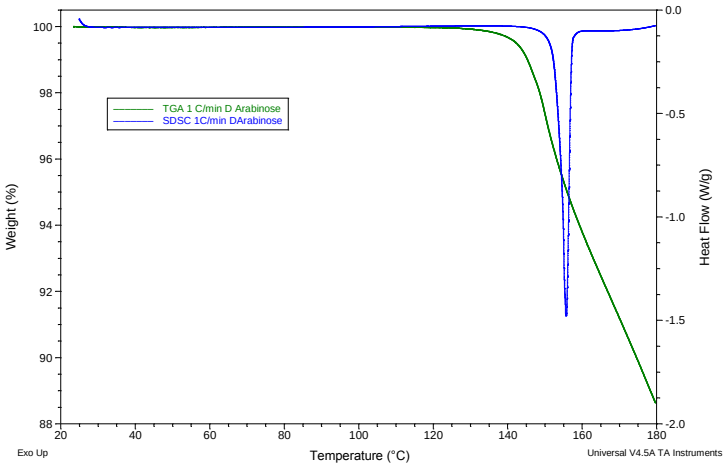

Figure 4-11: D Arabinose SDSC and TGA overlay at 1°C/min

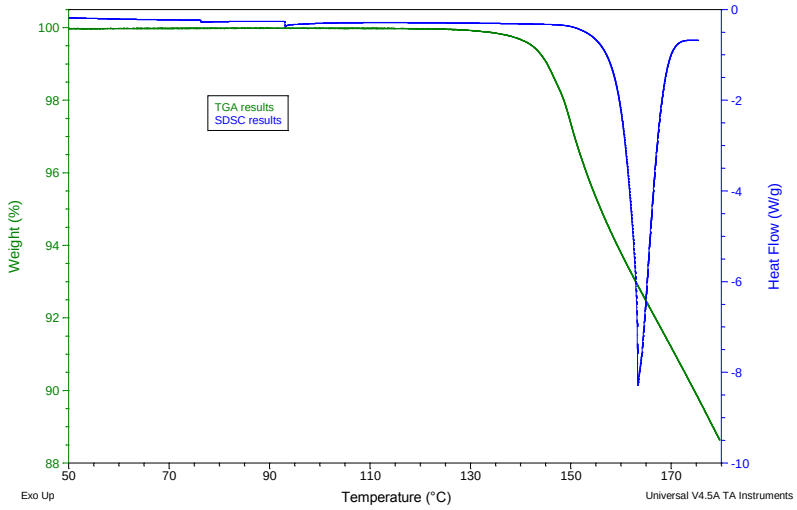

Figure 4-12: L Arabinose SDSC and TGA Overlay at 1°C/min

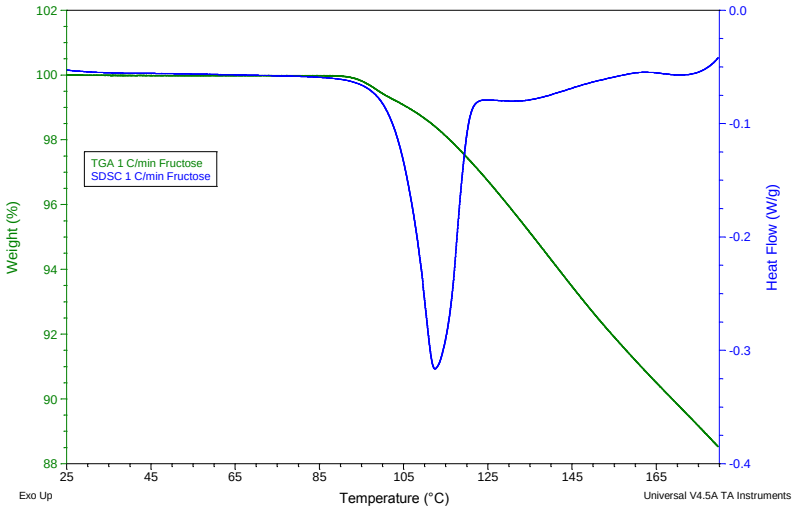

Figure 4-13: Fructose SDSC and TGA Overlay at 1°C/min

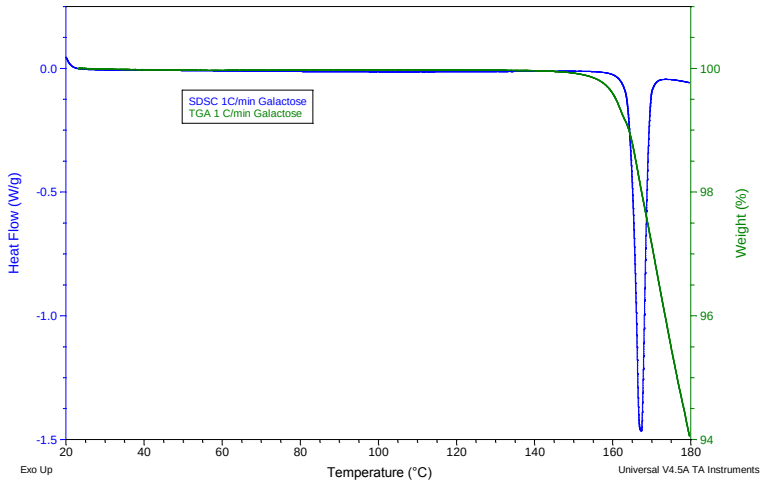

Figure 4-14: Galactose SDSC and TGA Overlay at 1°C/min

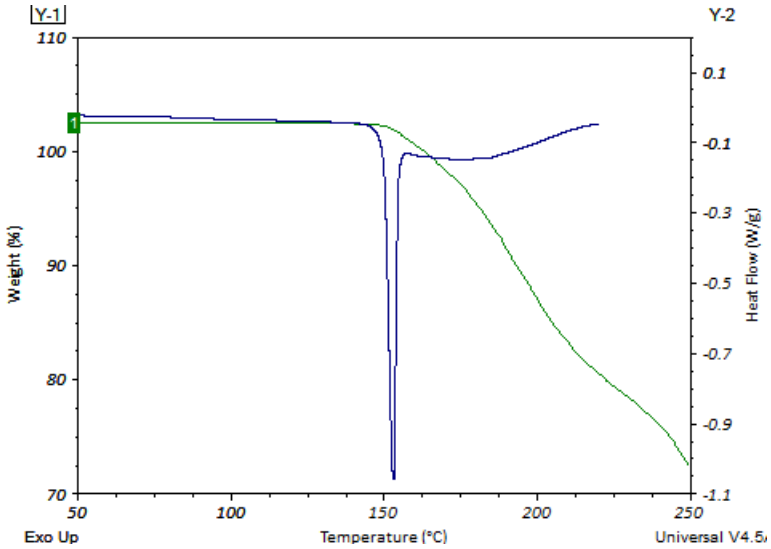

Figure 4-15: Glucose anhydrous SDSC and TGA Overlay at 1°C/min

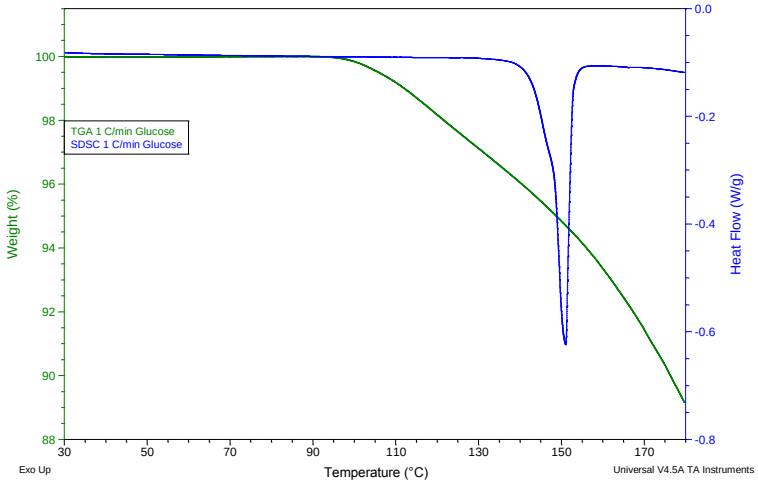

Figure 4-16: Glucose monohydrate SDSC and TGA Overlay at 1°C/min

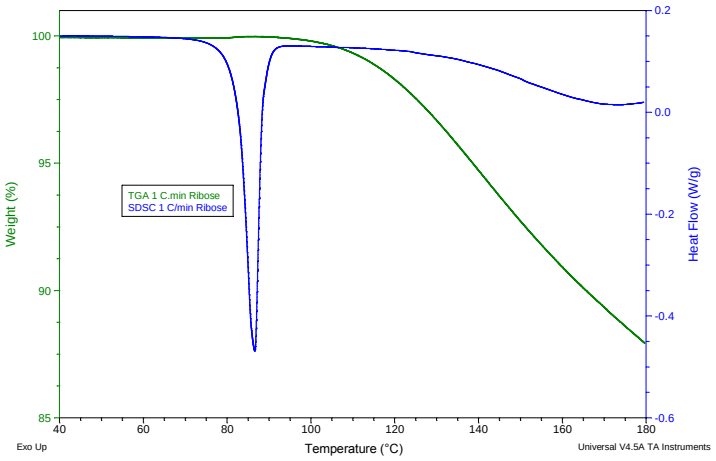

Figure 4-17: Ribose SDSC and TGA Overlay at 1°C/min

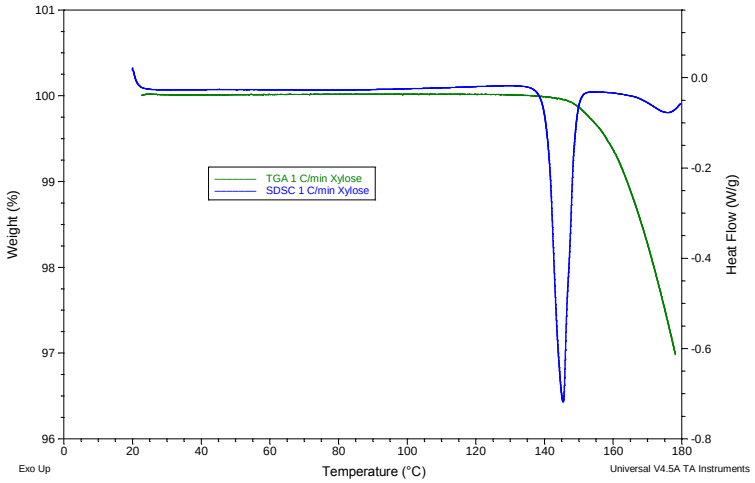

Figure 4-18: Xylose SDSC and TGA Overlay at 1°C/min

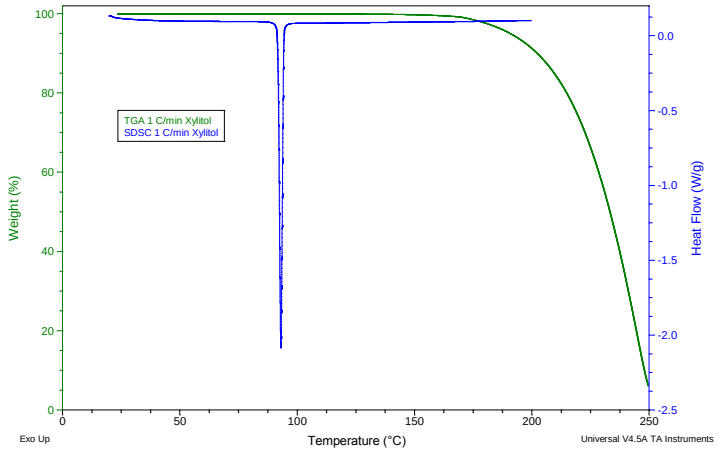

Figure 4-19: Xylitol SDSC and TGA Overlay at 1°C/min

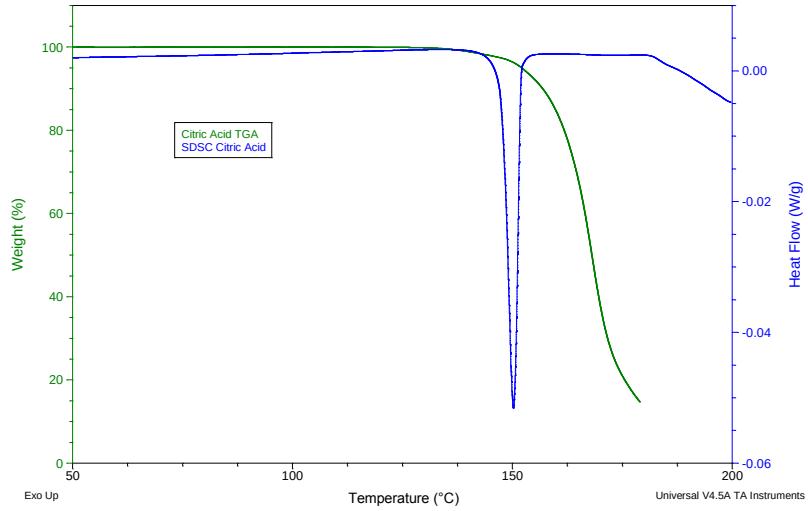

Figure 4-20: Citric Acid SDSC and TGA Overlay at 1°C/min

Table 4-1: Temperature range used in Stepwise Quasi-isothermal Experiments

Material	Temperature Range °C
D-Arabinose	130-145
L-Arabinose	130-145
Fructose	80-150
Galactose	140-200
Glucose anhydrous	120-180
Glucose monohydrate	120-180
Ribose	60-110
Xylose	120-180
Xylitol	70-110
Citric acid	120-180

Table 4-2: Tm Onset from MDSC

Material	Tm Onset °C as measured by MDSC 1°C/min modulation 1°C for 100 seconds	Standard deviation
D - arabinose	150.59	1.08
L - arabinose	149.73	1.73
Glucose anhydrous	Not tested	
Glucose monohydrate	148.06	0.19
Fructose	105.09	0.79
Galactose	166.19	0.16
Ribose	78.80	2.15
Xylose	140.84	0.07
Xylitol	92.17	0.25
Citric Acid	148.71	0.07

Table 4-3: Temperature and Cp Results from Stepwise Quasi-Isothermal Experiment

Material	Onset Tm °C	St Dev	Onset Cp (J/g)	St Dev	Final Tm °C	St Dev	Final Cp (J/g)	St Dev	delta T °C	delta Cp (J/g)
D-Arabinose	130.99	0.51	1.32	0.16	136.99	0.01	2.12	0.69	6.66	0.79
L-Arabinose	132.99	0.50	0.55	0.13	134.99	0.02	1.71	0.38	2.00	1.16
Fructose	94.66	0.49	1.96	0.10	100.99	0.04	3.01	0.07	6.34	1.05
Galactose	148.65	0.52	2.44	0.12	150.99	0.01	3.59	0.13	2.33	1.15
Glucose Anhydrous	134.44	0.44	2.05	0.36	139.47	1.06	2.98	0.51	4.84	0.94
Glucose Monohydrate	134.43	1.01	2.26	0.12	140.26	0.58	3.38	0.22	5.83	1.12
Ribose	74.19	1.48	1.74	0.19	81.97	0.01	2.61	0.21	7.78	0.87
Xylose	125.65	0.50	2.44	0.37	131.64	0.50	3.72	0.48	6.00	1.29
Xylitol	90.75	0.44	2.71	0.27	93.97	0.01	3.22	0.19	3.22	0.51
Citric Acid	132.98	1.23	1.33	0.71	146.98	0.01	2.08	0.95	14.00	0.74

Table 4-4: Summary of the shape of the Quasi-isothermal signal of Reversing Heat Capacity (Cp) Delta T and Delta Cp

Material	Shape of signal of Rev	delta T (°C)	St Dev	delta Cp	St Dev
D-Arabinose	S Curve	6.66	0.51	0.79	0.54
L-Arabinose	S Curve	2.00	0.51	1.16	0.30
Fructose	S Curve	6.34	0.50	1.05	0.60
Galactose	S Curve	2.33	0.52	1.15	0.50
Glucose Anhydrous	S Curve	4.84	1.25	0.94	0.15
Glucose	S Curve	5.83	1.38	1.12	0.12
Ribose	S Curve	8.00	1.48	0.83	0.04
Xylose	S Curve	6.00	0.50	1.29	0.11
Xylitol	Up and back	3.22	0.44	0.51	0.17
Citric Acid	???	14.00	1.23	0.74	0.24

Table 4-5: Ti Onset of Weight Loss in TGA Calculated by TA software using the full TGA results

Material	Ti (°C) at 1°C/min	Standard Deviation	Ti (°C) at 5°C/min	Standard Deviation	Ti (°C) at 10°C/min	Standard Deviation	ΔTi (°C) from 1°C/min and 10°C/min
D-Arabinose	147.17	2.42	157.42	4.61	161	5.46	13.83
L-Arabinose	151.98	4.78	161.56	1.65	164.08	1.13	12.11
Fructose	104.7	3.75	140.07	1.56	139.24	0.98	34.54
Galactose	162.93	4.2	183.2	1.42	182.64	2.1	19.71
Glucose anhydrous	165.52	7.1	188.55	2.57	202.52	6.67	37
Glucose monohydrate	158.55	1.33	162.69	2.45	163.9	0.83	5.35
Ribose	123.73	10	157.32	1.58	157.91	2.04	34.17
Xylose	157.15	2.57	163.53	0.51	179.95	0.26	22.81
Xylitol	216.52	2.1	219.17	3.29	214.93	5.08	-1.7
Citric Acid	164.22	1.76	161.64	3.99	163.75	2.52	-0.47

Table 4-6: Summary of Temperature at 0.1% weight loss and Ti onset using 0.1% weight loss

Material	Heating Rate °C/min	T in °C at 0.1% weight loss	STDEV	Calculated Onset Ti in °C using T at 0.1% weight loss	STDEV
D-Arabinose	1	133.56	1.79	128.46	1.38
	5	149.09	0.11	140.77	0.23
	10	155.83	0.97	150.54	0.47
L-Arabinose	1	140.48	8.36	135.51	8.52
	5	155.13	8.78	145.45	5.32
	10	152.77	2.33	145.60	5.10
Fructose	1	96.07	3.10	92.94	2.04
	5	122.40	0.87	116.99	1.51
	10	123.14	3.03	119.20	4.07
Galactose	1	133.37	1.14	150.20	1.31
	5	170.08	0.48	163.98	1.71
	10	181.20	1.51	174.08	2.23
Glucose anhydrous	1	146.49	0.71	139.49	3.51
	5	161.82	0.87	158.13	3.55
	10	172.39	0.87	167.52	2.59
Glucose monohydrate	1	134.32	27.47	127.70	26.44
	5	165.73	1.37	157.68	1.07
	10	174.61	1.00	163.67	0.59
Ribose	1	101.09	4.31	95.81	3.56
	5	127.99	6.03	120.05	4.64
	10	134.88	4.32	126.55	9.63
Xylose	1	139.82	6.68	132.74	7.68
	5	154.91	0.82	146.62	1.89
	10	162.64	0.29	149.23	1.64
Xylitol	1	137.27	5.84	129.03	4.24
	5	158.29	6.42	147.70	10.23
	10	166.90	6.14	153.47	4.36
Citric Acid	1	144.63	5.54	142.83	5.06
	5	159.63	0.42	154.78	0.30
	10	138.91	3.43	144.68	2.53

Table 4-7: Comparison of Tm onset from SDSC, MDSC and Ti at 0.1% weight loss from TGA at a heating rate of 1°C/min

Material	Tm onset melting SDSC (°C) obj. 1	Tm onset melting (°C) MDSC obj. 2	Ti onset decomposition (°C) TGA
D-Arabinose	153.62	150.59	147.17
L-Arabinose	154.24	149.73	151.98
Fructose	104.98	105.09	104.70
Galactose	164.62	166.19	162.93
Glucose anhydrous	149.33	Not tested	165.52
Glucose monohydrate	147.32	148.06	158.55
Ribose	82.15	78.80	123.73
Xylose	141.23	140.84	157.15
Xylitol	91.49	92.17	216.62
Citric acid	147.79	148.71	164.22

Table 4-8: Comparison of Ti onset to Literature Values

Material	Ti onset	Ti onset .1%	Heating Rate	Lit Ti onset	Heating Rate	Source
D-Arabinose	147.17	128.46	1°C/min	118.00	2°C/min	Räisänen et al. (2003)
l-Arabinose	151.98	140.77	1°C/min	147.00	2°C/min	Räisänen et al. (2003)
Fructose	104.70	92.94	1°C/min	116.30	1°C/min	Hurtta et al. (2004)
Galactose	162.93	150.20	1°C/min	152.0	10°C/min	Ramos-Sanchez et al. (1988)
Glucose anhydrous	165.52	139.49	1°C/min	149.80	1°C/min	Hurtta et al. (2004)
Glucose monohydrate	158.55	127.70	1°C/min	152.00	1°C/min	Hurtta et al. (2004)
Ribose	123.73	95.81	1°C/min	90.0	10°C/min	Ramos-Sanchez et al. (1988)
Xylose	157.15	132.74	1°C/min	148.00	2°C/min	Räisänen et al. (2003)
Xylitol	216.62	129.03	1°C/min	147.00	1°K/min	Lappalainen et al. (2006)
Citric Acid	164.22	143.83	5°C/min	148.00	5°C/min	Barbooti and Al-Sammerrai (1986)

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CHAPTER 5

Detection of Decomposition Components and Loss of Crystalline Structure in Select Monosaccharides held Isothermally at Low Temperatures

Abstract

Fructose, galactose, glucose monohydrate, sucrose and xylose were each held at a temperature below their measured Tm onset value for various times. Visual inspection of the samples, reversing heat capacity (Cp), monosaccharides retention and the HMF and furfural of each sample were measured. Sugar retention was measured by HPLC. HMF and furfural were selected as decomposition indicator compounds and were detected by HPLC. Each of the sugars tested showed an increase in reversing Cp, a development of a yellow color within the sugar crystal, a decrease in the amount of sugar present, and an increase in HMF and furfural with increasing time at the isothermal temperature. The sugars showed the decomposition indicator compound (HMF or furfural) being identified after 20% of the stabilization of heat capacity in all cases. Each of these factors (visual appearance, reversing Cp, decomposition products) indicate decomposition occurs under measured melting temperature, and the loss of crystalline structure is caused by the onset of thermal decomposition. Xylitol was held at its melting temperature (94°C) for 1000, 2000, and 3000 minutes. Holding xylitol at 94°C did not show any change in heat capacity, or loss in xylitol during any of the three holding times. Decomposition products were not detected validating that xylitol did not decompose.

Introduction

Results in Chapter 3 showed a heating rate dependence of the DSC Tm onset for each of the sugars tested (D-arabinose, L-arabinose, fructose, galactose, glucose anhydrous, glucose monohydrate, lactose anhydrous, lactose monohydrate, lactulose, maltose, mannose, panose, raffinose, ribose, sucrose, tagatose, trehalose and xylose). Results for citric acid were inconclusive. Results in Chapter 4 of the modulated quasi isothermal MDSC and the overlay DSC and TGA indicated that decomposition was taking place and that the materials were chemically changing during the melting process. This agrees with Lee et al. (2011a) who showed sucrose, glucose and fructose to be apparent melting materials. In apparent melting materials, the onset of melting is influenced by the onset of a kinetic process. The results in Chapter 4 indicate that the kinetic process is thermal decomposition, but do not

conclusively prove that decomposition is occurring. Typically, decomposition can be demonstrated by the identification of degradation compounds (Maga, 1989). Separation is usually done by GC or HPLC with identification of the degradation compounds done using one of the standard detectors. Additional detectors such as mass spectrometry can give information to identify the materials present during the decomposition reaction (Fagerson, 1969). A loss in the original compound can also be observed to determine if decomposition is occurring (Lee et al., 2011b).

The decomposition of sugars is marked by the identification of two major compounds, HMF (4-dydroxy-5-methly-3(2H) furanone) commonly called 5-(Hydroxymethyl) furfural and Furfural (Furan-2-carbaldehyde). The structures of these two compounds are show in Figure 5-1. HMF is the main degradation compound for the hexoses (glucose, galactose, fructose) (Blank and Fay, 1996). HMF is formed via a triple dehydration occurring in a hexose sugar. The formation of HMF from a hexose follows two simultaneous pathways (Lewkowski, 2001) as seen in Figure 5-2. Both reactions are complicated and can involve many intermediates (Clarke et al., 1997; Kelly and Brown, 1978; Orsi, 1973; Räisänen et al., 2003). The large number of intermediates makes it difficult to identify the early decomposition of hexoses and pentoses. Furfural is the main degradation compound for pentoses (xylose) and is formed by the triple dehydration of pentoses or from the loss of carbon from HMF (Fagerson, 1969). HMF could also further decompose to levulinic acid and formic acid; a schematic of the decomposition pathway with just the basic steps can be seen in Figure 5-3. The decomposition pathway can also result in the formation of oligosaccharides via polymerization (such as soluble polymers or humic acid), (Golon and Kuhnert, 2013; Heyns et al., 1966).

In order to ensure confirmation of the kinetic reactions taking place in the heating of sugars, decomposition products need to be identified. Thus, the research herein holds sugars at various times at a single temperature identified in the Chapter 4 as the temperature of stabilization of the reversing heat capacity. Detection of decomposition components and loss in crystal structure in fructose, glucose, galactose and xylose held isothermally by quasi-isothermal modulated DSC. The visual observations, reversing heat capacity and HPLC identification of initial sugar as well as decomposition indicator compounds will be studied to identify if decomposition has occurred at these temperatures.

Materials

Four materials were selected from Chapter 4 to further prove they are “apparent melting” materials: galactose, xylose, fructose, and glucose. In addition, Sigma sucrose was added so as to verify

the method and HPLC, because sucrose was used in the original research by Lee et al. (2011b). Xylitol was also added as a comparison material, to assess if thermodynamic melting materials behave differently under long hold times. Details on composition, lot number and supplier of each of the sugars and xylitol can be found in Table 3-1.

Methods

Quasi-isothermal MDSC: Hold below Tm Onset

Quasi-isothermal MDSC was performed using the modulated mode on the DSC Q2000. The instrument was calibrated using a sapphire disk (PN 970370.901, TA Instruments, New Castle, DE). Dry nitrogen purge gas was set at a flow rate of 50 mL/min. A modulation amplitude of ± 1.0^{o}C and a period of 100 sec was applied throughout the holding time. The isothermal temperature was determined by identifying the temperature at which the reversing heat capacity stabilized using the stepwise quasi-isothermal temperature in the previous experiment (Chapter 4). Data was collected after a five minute data off period for initial equilibration at each temperature. All sample measurements were done in triplicate.

Isothermal temperature for each sample is displayed in Table 4-3. The final temperature from this table was used in the experiments herein. The final temperature was determined to be the temperature at which the reversing Cp stabilized during the stepwise quasi-isothermal MDSC experiment. A preliminary experiment was run to determine the time it takes for the reversing Cp to stabilize at the holding temperature from Table 4-3. The first experiment was conducted by holding the sample at the final temperature for an extended period of time (1400 minutes). The long hold time was found to be long enough to include decomposition events for each of the compounds. The reversing heat capacity from these results was then plotted as a function of time. The plot of heat capacity versus time was then evaluated; the time at which the reversing heat capacity levels off is called “full time”. Figure 5-4 shows the reversing Cp plotted as a function of temperature. The temperature at which the reversing Cp levels off is labeled here with a red arrow. The time indicated is called “full time”. The following hold times (10%, 20%, 25%, 50%, 75%, 100% (full time) and 200%) were then calculated by multiplying the hold time at 100% times the percent required for each step. Samples of 5mg were held in the DSC for these times and collected to be run on the HPLC.

Table 5-1 shows the times and temperatures used for each of the sugars in the study. Each of the sugars was held below the Tm onset for the seven hold times. The final reversing Cp for each of the holding temperatures was recorded and averaged. The standard deviation was determined using Microsoft Excel®. After the samples were run on the DSC, the pans were opened and pictures were taken of the samples. Pictures were taken with natural lighting using an IPhone camera in the laboratory.

HPLC: Sugars

Identification of the thermally treated sugar samples was done using HPLC based on AOAC Official Method 996.04. Carbohydrates (sugars and any decomposition artifacts) were separated by anion exchange chromatography and detected by pulsed amperometric detection at a gold working electrode. A Dionex IC3000 HPLC was equipped with a gradient pump, Dionex Carbopac PA1 guard and analytical columns and an electrochemical detector with disposable carbohydrate-certified gold electrodes. A 150mM solution of sodium hydroxide was used as the eluent at a flow rate of 1.0 mL/min and a column temperature of 30°C. Limit of detection for the sugars was 0.5 ppm. The main compound (i.e. fructose, glucose, galactose, sucrose, or xylose) was recorded and any breakdown products which are known mono and disaccharides (i.e. fructose and glucose in the case of sucrose) were also recorded.

HPLC: HMF and Furfural

HMF and furfural were separated from other UV absorbing compounds on a C8 Reversed Phase HPLC column (Microsorb-MV 100A Cat No R0086300E3 from Varian) and were quantified with UV detection at 282 nm (Waters Model 2487 Dual Wavelength Absorbance Detector (Cat. # WAT 081110. Single Wavelength Noise Level less than 0.35 X10-5 AU). A Waters model 515 isocratic pump (Cat. # WAT 207000) and a Waters Model 717 plus auto-sampler (Cat. # WAT 207144, with at least a 350 microliter loop installed) were used. A C18 guard column (Cat No. R0080200G3 from Varian) was used to protect the main column. Under the conditions of this procedure, the detection limits for HMF and furfural were 50 ppb. Flow rate was 1 mL/min with 10% acetonitrile/0.1% acidified water solution. The water was acidified with 85% phosphoric acid. HMF (4-dydroxy-5-methly-3(2H) furanone) is a main degradation compound for the hexoses (glucose, galactose, fructose) (Blank and Fay, 1996). Furfural is a detectable decomposition compound for pentoses. Results were reported in ppm.

Results and Discussion

All of the sugars showed a decrease in concentration during the time and temperature combinations. The sugar content decreased and the HMF and furfural increased. For hexoses (fructose, galactose, and glucose) HMF is the first indicator compound. When the hexose begins to decompose, there can be several different intermediates, but all of the hexoses include HMF as an intermediate. HMF content is not stable once it is created. Some of the HMF is converted to an ether, some is condensed into polymers, and some is further decomposed, eventually leading to levulinic acid and formic acid. Because there are so many pathways and intermediates, there is not a one-to-one relationship between the decrease in sugar content and the increase in HMF. However, as an indicator compound, HMF is an early decomposition material, easy to detect, and present in all hexose decomposition. Selecting HMF as an indicator compound would also include detecting decomposition in xylitol. Xylitol decomposition also includes HMF in its pathway, since it will also lose three water molecules. For pentoses (xylose) furfural acts as the indicator compound. It also is an early decomposition product, which is easy to detect and is present in both the pentose decomposition pathway, as well as a further decomposition product in the hexose decomposition pathway. All the data for the graphs are provided in Appendix A. The behavior of each of the sugars is discussed in-depth independently below.

Sucrose

Sucrose samples were held at 132°C for seven hold times as reported in Table 5-1. The lowest literature value for DSC Tm onset is 160°C (Raemy and Schweizer, 1983) and lowest value from this research is 161°C. The results for the reversing Cp and standard deviations are given in Table A-1. Figure -5-5 visually shows the sucrose crystals as they were held for various times. An examination of the samples shows that a yellow color is visible after 480 minutes, but the crystals retain their original morphology with the external crystal structure still intact. Crystals at 720 minutes are beginning to lose their external crystalline structure and are more visibly yellow. There is still a small amount of intact crystal structure visible at 960 minutes with a strong yellow color. At 1920 minutes the external crystal structure is completely missing, and the color has changed to brown. Reversing Cp results are plotted in Figure 5-6. Viewing the HPLC results in Figure 5-7, the trend of decreasing sucrose and increasing HMF and furfural over time can be seen. The HPLC results show that the amount of sucrose decreases with increasing time; even a hold time of 96 minutes begins to lose sucrose and increase glucose and fructose

as reported in Table A-6. HMF and furfural are detectable even in the samples held at the shortest time (96 minutes). At 1920 minutes, the amount of glucose and fructose begins to decrease as more of it has been converted to HMF and furfural.

In the work by Lee et al. (2011b) sucrose was held at 120°C and initial HMF and glucose were detected at 50 minutes and was correlated to an increase in Cp though individual values were not reported. In this study, the sucrose was held at a slightly higher temperature (132°C compared to 120°C) but the first time point measured was at 96 minutes. However, an increase in Cp was not observed until 240 minutes. The time point of 96 minutes did show glucose and HMF. The shape of the reversing Cp curve was the same in both experiments, but at the lower temperature (120°C) the initial baseline was longer. These results confirm the use of the ability to detect decomposition in sucrose when it is held for extended periods at a temperature below its reported melting temperature. The results also confirm that the loss in crystal structure in sucrose is a time/temperature combination process. This isothermal technique can be used for the other sugars.

Fructose

Fructose was held at 101°C for various times as reported in Figure 5-1. The lowest temperature for the loss in crystal structure for fructose found in this research is 105°C. Literature has reported melting temperatures as low at 80°C determined by heat flow calorimeter at 1°C/min (Raemy and Schweizer, 1983). Fructose pictures seen in Figure 5-8 show very little yellow color developed and an almost immediate decrease in crystalline fructose. Results for the average reversing Cp from each of the run times are reported in Table A-2 and plotted in Figure 5-9. The results show an increase in reversing Cp with an increase in hold time as in the other sugars. Fructose, unlike the other sugars, is very hygroscopic and can liquefy using moisture from the air. Figure 5-10 plots the HPLC results for fructose and HMF, and the results are tabulated in Table A-7. There was both HMF and furfural detected in the zero time samples. This could show some thermal abuse. The HMF begins to increase from the time zero value at the third time point (33.75 minutes). At the full time sample (135 minutes), the HMF starts to substantially increase, and at that time the decrease in fructose is also observed. The fructose samples displayed a reversing Cp with a slightly different shape than the other sugars. The fructose Cp did not demonstrate an initial “lag” phase; no baseline value for Cp was observed. In fructose, the Cp started to change immediately during the holding. This corresponds with the visual pictures which show a loss in crystalline structure occurring in the second time period (27 minutes). Decomposition indicator

materials in fructose samples were detected when the crystal structure was still intact and before any yellow color was observed. The loss in crystal structure occurred early in the holding of fructose samples, as was seen visually and by the reversing Cp.

Galactose

Galactose was held at 151°C for various times as reported in Table 5-1. The lowest Tm onset for the galactose in this research was 164°C. The lowest reported literature value for galactose was 140°C determined by heat flow calorimeter at 1°C/min (Raemy and Schweizer, 1983). Looking at the pictures of galactose held at 151°C seen in Figure 5-11, the beginning of yellow color can be seen after 31 minutes. At 116 minutes, more yellow is seen, and the crystals look like they are beginning to lose their crystalline structure, slightly. At 155 minutes, the color has started to darken significantly, but there is still evidence of some crystalline structure. A reversing Cp signal of each of the runs for galactose is shown in Figure 5-12. The overlay of the plots of reversing Cp shows each of the runs has good correlation and exhibit the S-curve shape. Results for the average reversing Cp from each of the times are reported in Table A-3. Galactose, HMF and furfural as determined HPLC are seen in Figure 5-13 and reported in Table A-8. For galactose, the HMF levels increase almost immediately (at the 10% time point), and continue to increase in level at each time point. Furfural does not accumulate until after 155 minutes. The amount of galactose does not appreciably change until after 155 minutes. The decomposition indicator compounds are present before the development of yellow color can be seen visually. The pictures, reversing Cp plots and HPLC results show galactose decomposes when held isothermally under the melting temperature at 151°C.

Glucose Monohydrate

Glucose monohydrate was held at 140°C for various times as reported in Table 5-1. The lowest temperature reported in this research for Tm onset was 147°C (1°C/min), the literature reports 143°C as the lowest melting temperature (Roos, 1993). The pictures of glucose monohydrate held at 140°C in Figure 5-14 do not show a high degree of yellowing. After holding for 82.5 minutes, some change in the samples is starting to be observed. At 110 minutes, there is slight yellow color, and the sample is mostly melted, though some crystalline structure is still observed. Results for the average reversing Cp from each of the run times are reported in Table A-4 and the plots are shown in Figure 5-15. The results show an increase in reversing Cp with an increase in hold time as it would be expected with a chemical change

in material. The curves also follow the S-curve shape observed in the other sugars (except fructose). The results for glucose content, HMF and furfural can be seen in Figure 5-16. Complete data can be seen in Table A-9. There is no increase in HMF until 55 minutes. At 82.5 minutes, there is significantly more HMF, and the HMF continues to increase for the rest of the holding times. Furfural is detected at 110 minutes at low levels, but more significantly at 220 minutes. Glucose content begins to decrease at 82.5 minutes. The color of the samples, the reversing Cp and the detection of HMF all show that decomposition occurs in glucose monohydrate at 140°C.

Xylose

Xylose was held at 132°C for various times as reported in Table 5-1. The lowest temperature for Tm onset found in the literature was 135°C (Raemy and Schweizer, 1983). In this research the lowest Tm onset was 141°C (1°C/min). Xylose pictures as seen in Figure 5-17 show a slight yellowing of the samples after 114.75 minutes. The samples continue to yellow until the samples liquefy at 459 minutes. Results for the average reversing Cp from each of the run times are reported in Table A-5 and plotted in Figure 5-18. The results show an increase in reversing Cp with an increase in hold time as like the other sugars following the S-curve shape. The heat capacity markedly changed at 459 minutes, the time where loss in crystal structure is seen in the pictures. The HPLC results in Table A-10 show the xylose content doesn't change significantly until about 229.5 minutes, after which it begins to decrease. At 229.5 minutes, the furfural has also begun to increase. These results can be viewed in Figure 5-19 and they are tabulated in Table A-10. The results show stability in the xylose for about 50% of the hold time (229.5 minutes), and a decrease in xylose after that time. Furfural is first detected at a hold time of 91.8 minutes and continues to increase during the holding. HMF is not made in the decomposition of xylose since xylose is a pentose. The pictures, reversing Cp and HPLC results all show that xylose decomposes when held isothermally at 132°C.

Xylitol

Xylitol was held at 100°C for 1000, 2000, and 3000 minutes. The longest time any of the sugars in this study was held isothermally was 1920 minutes (sucrose). Two thousand minutes was selected to be roughly equal to the longest hold time of sucrose. 3000 minutes would be a 50% longer time and 1000 would be half that time. Pictures in Figure 5-20 of the xylitol samples showed no color development regardless of the hold time. The pictures also showed all of the samples lost crystal

structure when held isothermally at the melting temperature. Throughout the three holding times no change in Cp was observed. The overlay plots for heat capacity are shown in Figure 5-21. The HPLC showed no HMF or furfural formed, and all the xylitol remained intact. The HPLC results are graphed in Figure 5-22 and tabulated in Table A-11. It was determined that no decomposition has occurred during these temperatures even after the very long holding times and the loss in crystal structure.

Comparison of Sugars

Sucrose, fructose, galactose, glucose monohydrate, and xylose were each held at a temperature below the measured Tm onset for various times. The reversing heat capacity (Cp) was reproducible between the runs for different hold times. The shape of the reserving heat capacity curves were the same for sucrose, galactose, glucose monohydrate, and xylose. All had the same S-curve shape repeatedly seen in this research. The fructose had a similar shape, but without an initial level baseline; the reversing heat capacity increases almost immediately. Visual inspection of the samples shows that sugars (except fructose) begin to develop a yellow color while the crystal structure is still intact. The pictures reveal that fructose loses its crystalline structure within 27 minutes. The quick loss in crystalline structure was seen in the immediate change in reversing heat capacity. The HPLC measured the monosaccharides and the HMF and furfural of each sample. The galactose and glucose monohydrate showed an appearance of initial decomposition components (HMF) at the first holding time measured (galactose at 15 minutes, glucose monohydrate at 11 minutes). Furfural was detected in xylose at the second time point, 91.8 minutes (20% hold time). Fructose had measureable amounts of HMF and furfural detected even in the initial samples, which shows the sample may have been heat abused, but HMF levels increased after 27 minutes (20% hold time). The three hexoses (fructose, galactose, and glucose monohydrate) had very similar hold times (135, 155, 110 respectively) to give a leveling of their reversing Cp. Xylose, the pentose, needed to be held at a longer time to reach the stable level of reversing Cp after the loss of crystal structure. Sucrose had the longest hold times, but it was held at a temperature below the loss in crystal structure reported in this research or in the literature (Lee et al., 2011a).

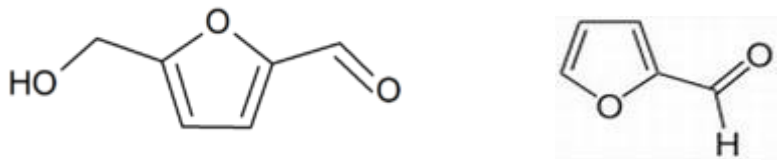
Xylitol had a level reversing heat capacity, no increase in HMF or furfural and no decrease in xylitol even through the very long holding times. It was found to be stable when held at the melting temperature.

Each of the sugars tested showed an increase in reversing Cp, a development of a yellow color within the sugar crystal, a decrease in amount of sugar present, and an increase in HMF and furfural with increasing time at the isothermal temperature. Each of these factors indicates that decomposition occurred before reported Tm onset had taken place.

Conclusions

The HPLC results demonstrate that each of the sugars (galactose, fructose, glucose monohydrate, xylose, and sucrose) decomposed slowly at the temperature under the melting temperature. Also the galactose, glucose monohydrate, xylose and sucrose showed a visible yellowing of the intact crystals. None of the sugars tested showed appreciable loss until after 50% of the hold time to stabilize the reversing Cp at the given temperature. Sucrose showed a decrease after 25% of the hold time. The first identifiable degradation compound (HMF for hexoses, and furfural for the pentose) appeared after holding for 10% of the time in the case of sucrose, galactose, glucose monohydrate, and fructose, and after 20% of the time in the case of xylose. Each of these sugars appears to be an apparent melting material, where the decomposition causes a loss in crystalline structure. The heat capacity data, visual observations and HPLC results show that all the sugars (sucrose, galactose, glucose monohydrate, fructose and xylose) decompose at temperatures under reported melting temperatures and are apparent melting materials as defined by Lee et al. (2011a). Xylitol did not change during the three holding times in this study. It did not show any decomposition at temperatures under the melting temperature.

Figures and Tables Chapter 5



HMF Furfural

Figure 5-1: Structure of two main decomposition products of carbohydrates (HMF and Furfural)

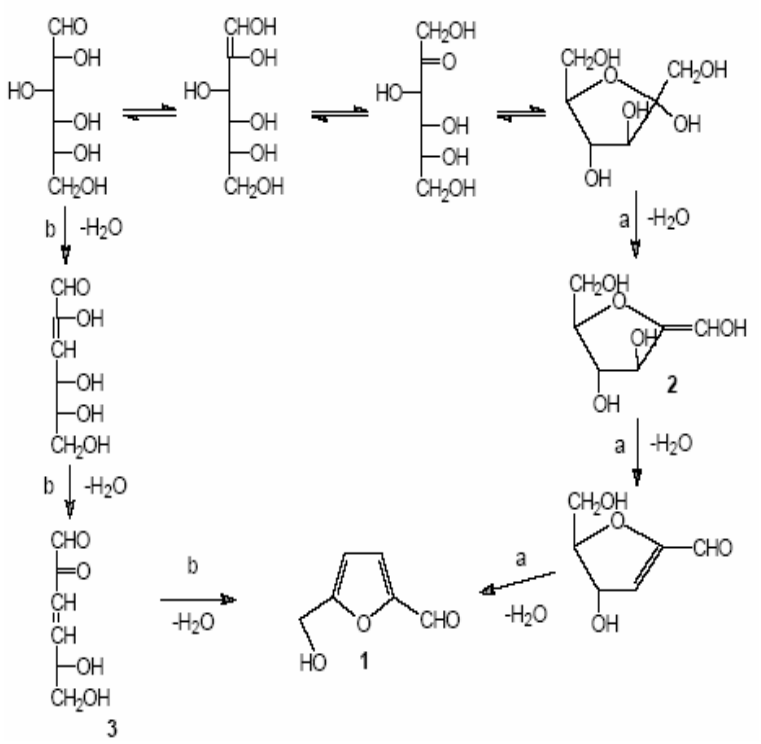


Figure 5-2: Linear and cyclic pathway to the formation of HMF (compound 1) from a hexose (excerpted from Lewkowski, 2001)

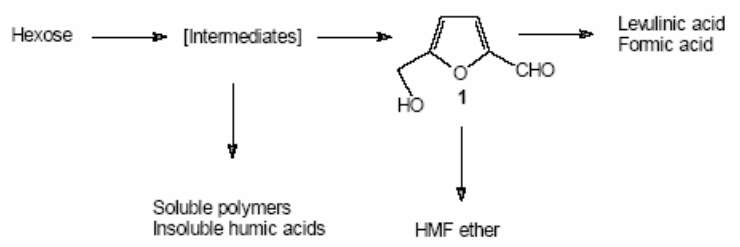


Figure 5-3: High level schematic of decomposition of a hexose (excerpted from Lewkowski, 2001)

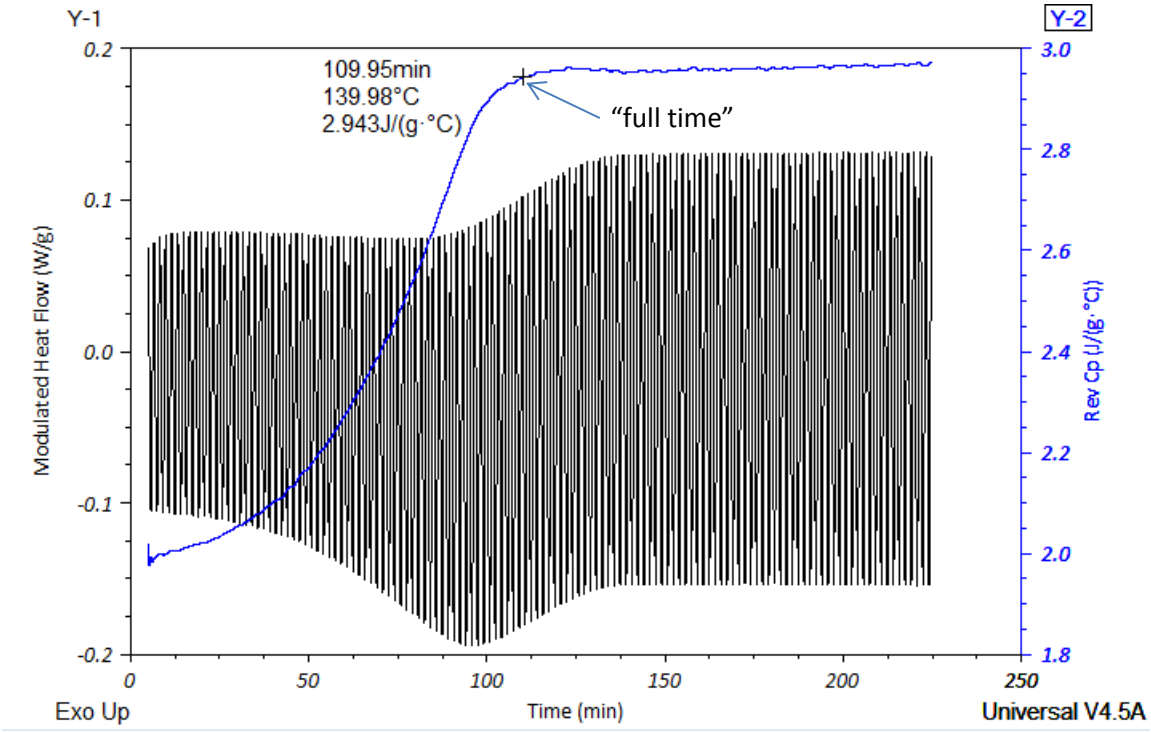


Figure 5-4: Reversing Cp signal for glucose monohydrate held at 140°C for 250 minutes in the quasi-isothermal MDSC. The arrow demonstrates "full time" and other hold times were determined from 110 minutes for the isothermal holding.

Sucrose Results

0 min 96 min 192 min 240 min 480 min 720 min 960 min 1920 min

Figure 5-5: Pictures of sucrose held at 132°C for various times

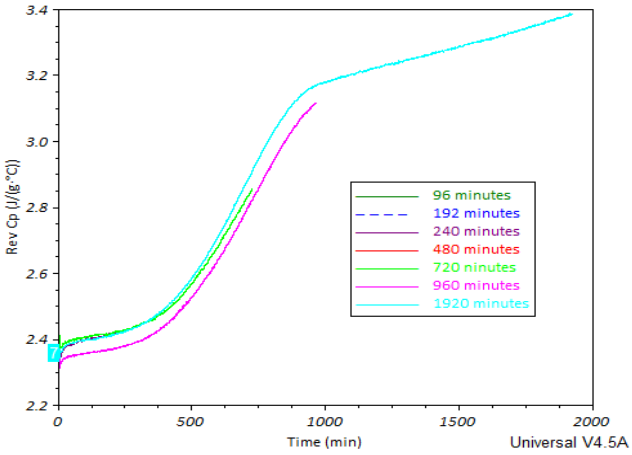


Figure 5-6: Reversing heat capacity of sucrose samples held at 132°C for various times

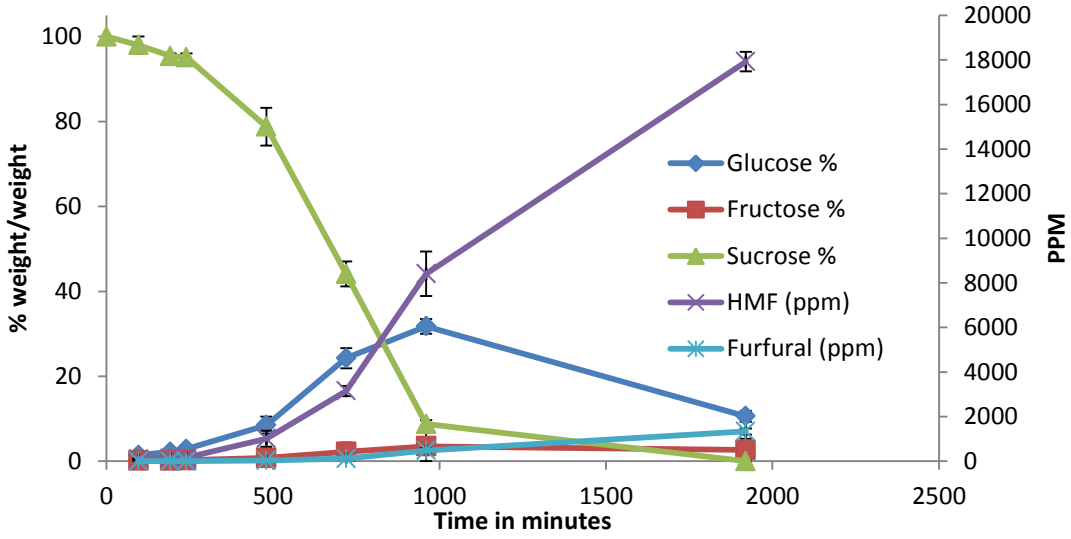


Figure 5-7: % Sucrose, glucose and fructose, HMF and Furfural in sucrose samples held at 132°C for various times

Fructose Results

0 min 13.5 min 27 min 33.75 min 67.5 min 101.25 min 135 min 270 min

Figure 5-8: : Pictures of fructose held at 151°C for various times

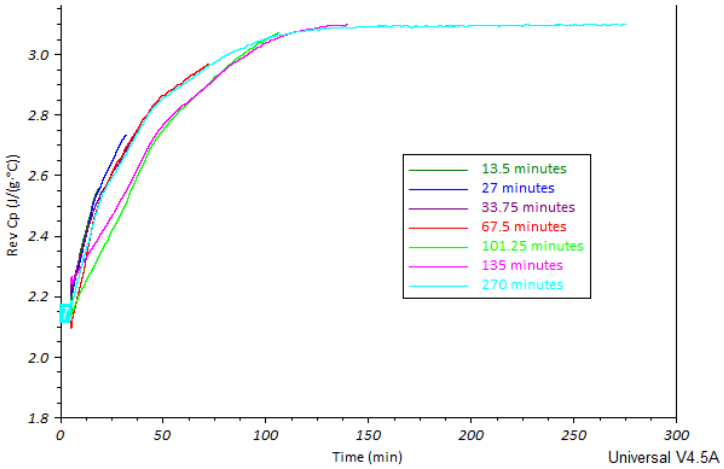


Figure 5-9: Reversing Cp of fructose held at 151°C for various times

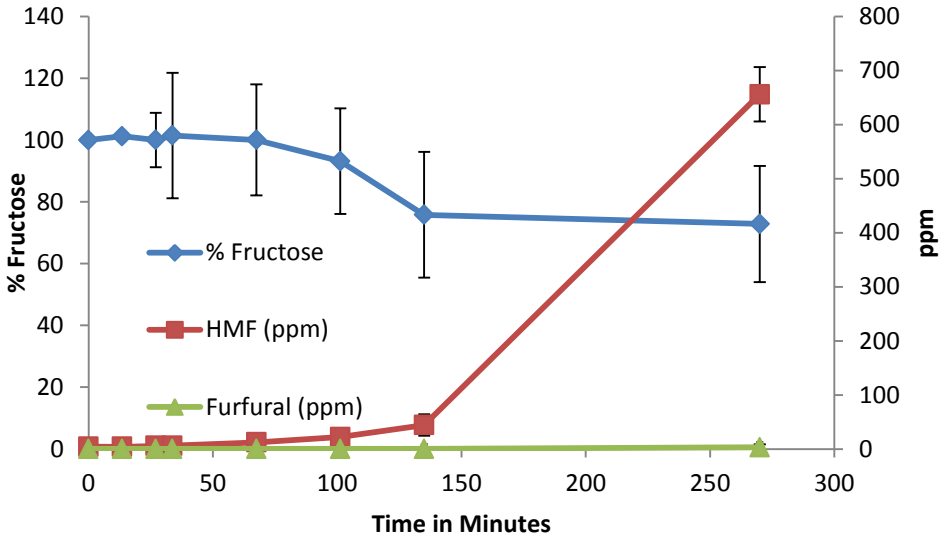
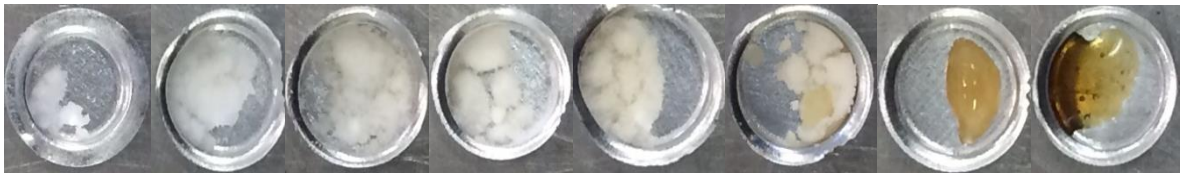


Figure 5-10: % Fructose, HMF and furfural in samples held for various times

Galactose Results



0 min 15.5 min 31 min 38.75 min 77.5 min 116.25 min 155 min 270 min

Figure 5-11: : Pictures of galactose held at 151C for various times

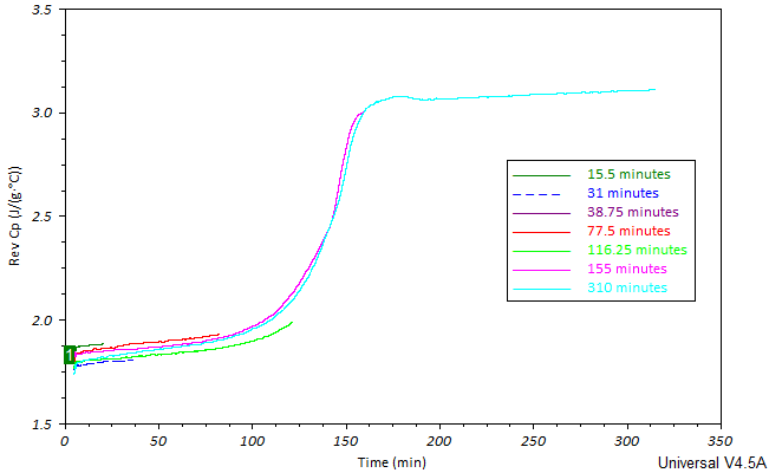


Figure 5-12: Reversing Cp curves of galactose held at 151°C for various times

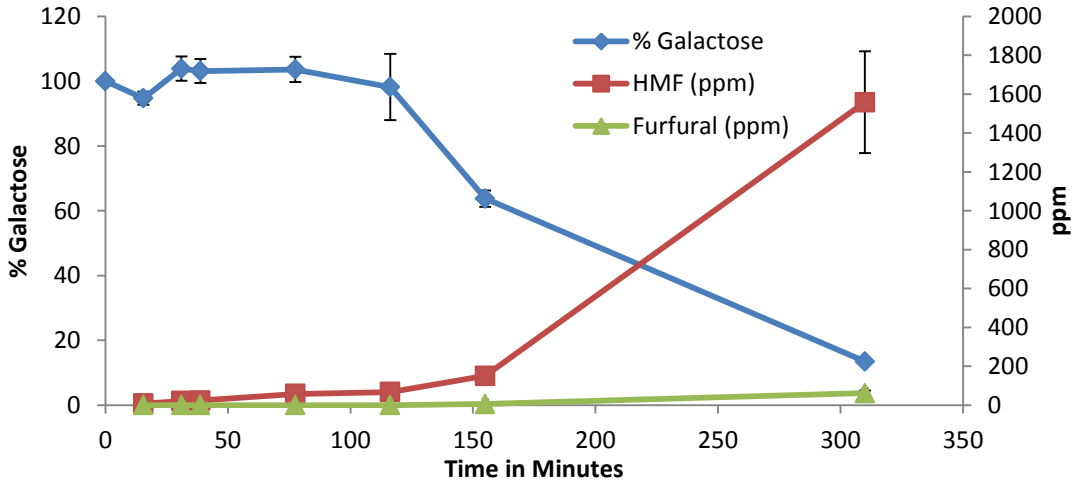
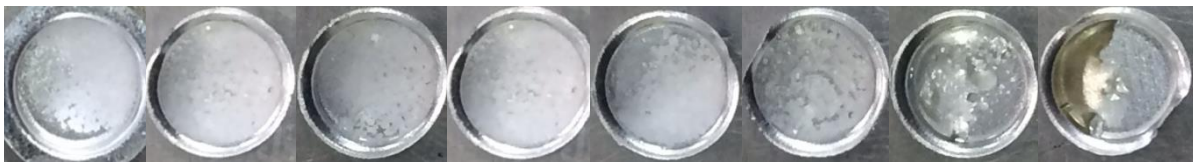


Figure 5-13: Galactose %, HMF and Furfural in galactose samples held at 151°C for various times

Glucose Monohydrate Results



0 min 11 min 22 min 27.5 min 55 min 82.5 min 110 min 220 min

Figure 5-14: Pictures of glucose monohydrate samples held at 140°C for various times

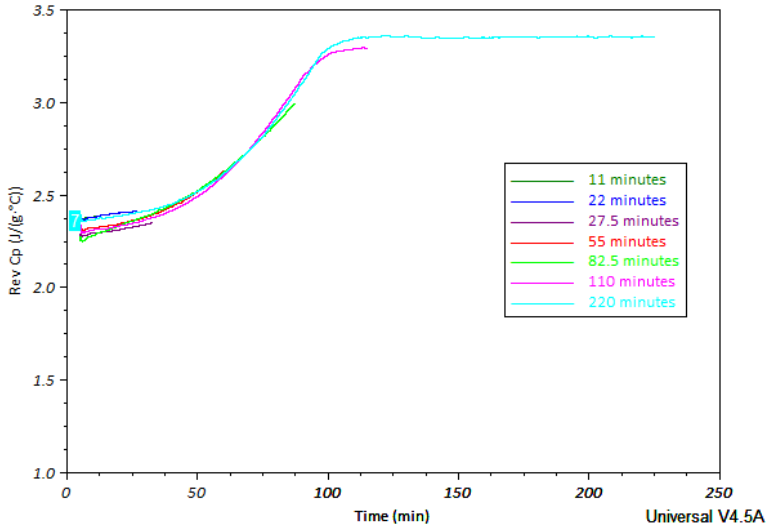


Figure 5-15: Reversing Cp of glucose monohydrate samples held at 140°C for various times

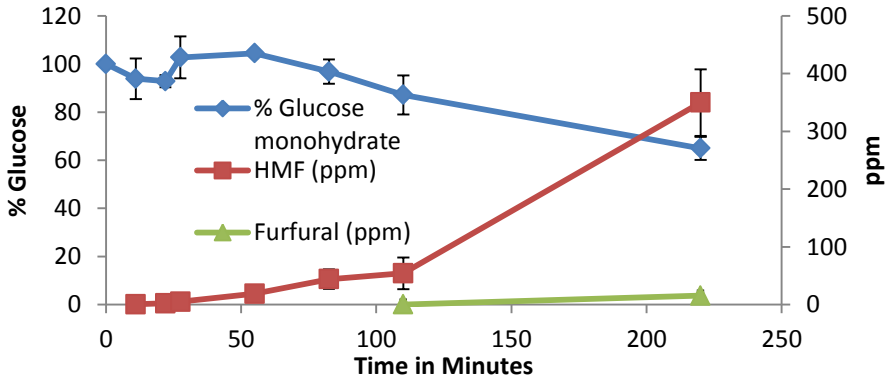


Figure 5-16: % Glucose monohydrate, HMF and furfural in samples held at 140°C for various times

Xylose Results

0 min 45.9 min 91.8 min 114.75 min 229.5 min 344.25 min 459 min 918 min

Figure 5-17: Pictures of xylose held at 132°C for various times

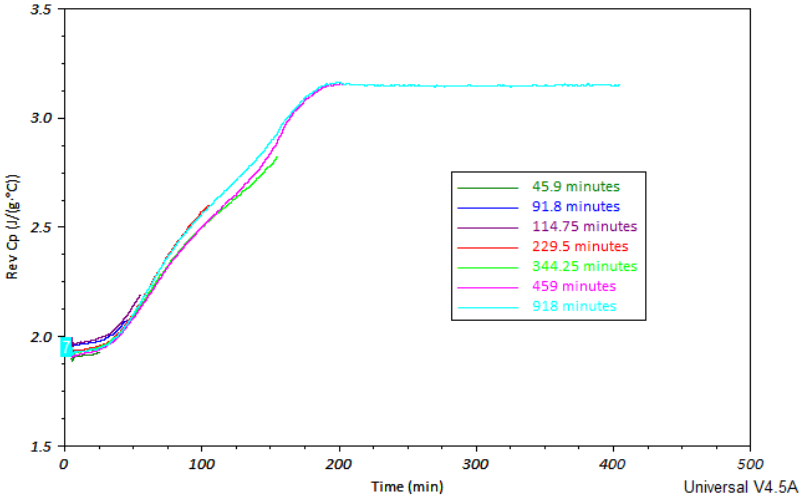


Figure 5-18: Reversing heat capacity of xylose samples held for various times

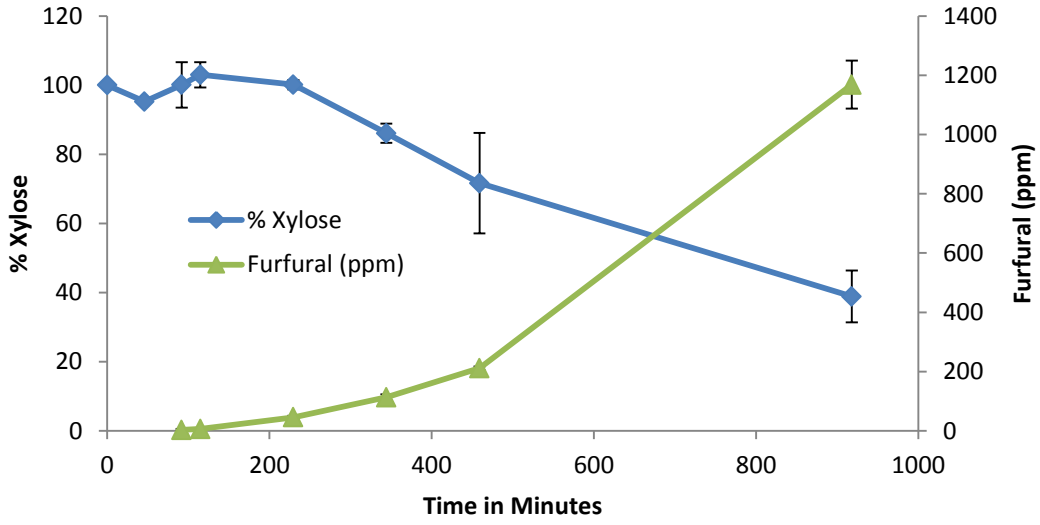


Figure 5-19: % Xylose and furfural in xylose samples held at 132°C for various times

Xyltiol Results

0 min 1000 min 2000 min 3000 min

Figure 5-20: : Pictures of xylitol held at 94°C for various times

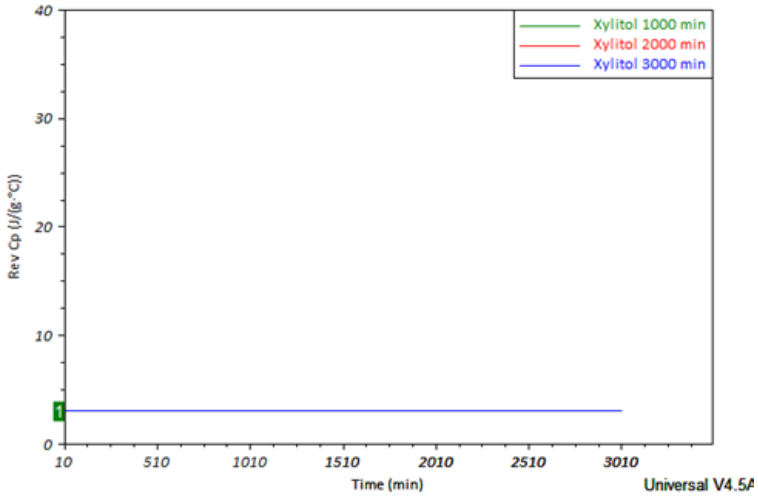


Figure 5-21: : Reversing heat capacity of xylitol samples held for various times

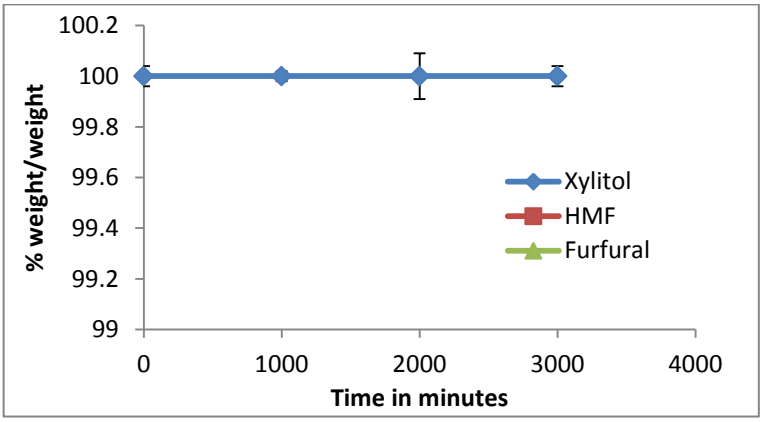


Figure 5-22: % Xylitol, HMF, and furfural in xylitol samples held at 94°C for various times

Table 5-1: Summary of Times and Temperature used in the DSC for decomposition experiment

Sugar	Time interval (%)	Hold Time in minutes	Temp °C
Fructose	10	13.5	101
	20	27	
	25	33.75	
	50	67.5	
	75	101.25	
	Full (100%)	135	
	Double (200%)	270	
Galactose	10	15.5	151
	20	31	
	25	38.75	
	50	77.5	
	75	116.25	
	Full (100%)	155	
	Double (200%)	310	
Glucose	10	11	140
	20	22	
	25	27.5	
	50	55	
	75	82.5	
	Full (100%)	110	
	Double (200%)	220	
Sucrose	10	96	132
	20	192	
	25	240	
	50	480	
	75	720	
	Full (100%)	960	
	Double (200%)	1920	
Xylose	10	45.9	132
	20	91.8	
	25	114.75	
	50	229.5	
	75	344.25	
	Full (100%)	459	
	Double (200%)	918	

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CHAPTER 6

Common Structural Features among Carbohydrate Materials that Result in Apparent Melting Behavior

Abstract

When comparing the apparent melting materials studied herein (xylose, glucose, fructose, sucrose, and galactose) to related thermodynamic materials (mannitol and xylitol), the major structural difference is the presence of a carbonyl group (aldehydes or ketones) compared to a hydroxyl group. Citric acid also contains a carbonyl group in the form of carboxylic acid, but the results for citric acid were inconclusive. The polyols (xylitol) have been reduced, and only contain hydroxyl groups. The polyols were demonstrated to be thermodynamic melting materials.

Discussion

Recent studies by Lee et al. (2011a) defined a new type of melting, termed apparent melting, where the loss of crystalline structure is associated with a kinetic process, specifically thermal decomposition, rather than thermodynamic melting. Since the melting temperature of these materials is being influenced by a kinetic event, the Tm onset (onset of melting) is heating-rate dependent. The three carbohydrate materials, sucrose, fructose, and glucose investigated by Lee et al. (2011a) exhibited apparent melting. In the same research, one carbohydrate type material, mannitol, was shown to exhibit a heating rate independent Tm onset. This type of melting was termed thermodynamic melting (Lee et al., 2011b). Lee et al. (2011a) showed that there is heating rate dependence for Tm onset and ΔH for fructose, glucose and sucrose, but not for mannitol. Lee et al. (2011b) demonstrated that decomposition products are detectable in sucrose at temperatures below the literature reported melting temperature using HPLC analysis.

In Chapter 3, twenty six materials were tested. All of the sugars tested (18), exhibited heating rate dependent loss in crystalline structure. None of the six polyols tested exhibited heating rate dependence for the loss in crystalline structure. In Chapter 4, nine sugars showed a S-curve pattern in the reversing Cp when slowly heated through the range of the loss in crystalline structure that indicated an irreversible chemical change in the material during heating and no ability to recrystallize. In Chapter

5, five sugars were confirmed to undergo decomposition by HPLC when held below their measured melting temperature. Each of the sugars tested showed decomposition products before a loss of crystal structure was observed visibly or in the reversing Cp.

Thermal decomposition of carbohydrates is a very complicated process with a number of intermediates and branches in the reaction scheme. In the decomposition pathway in monosaccharides, internal rearranging can occur, but the major pathway involves a triple dehydration of the monosaccharide resulting in HMF (or furfural in the case of pentoses). Lewkowski (2001) reports nearly 100 organic and inorganic compounds have been positively identified as catalysts to the formation of HMF. The first step of decomposition for disaccharides is a hydrolysis of the glyosidic linkage. After the disaccharide is separated into its component monosaccharides, the monosaccharides then generally follow the pathway to HMF. There are also condensation reactions that occur during decomposition that result in various oligosaccharides, such as humic acids.

A review of basic carbohydrate chemistry will facilitate understanding of the decomposition pathway. The use of the term carbohydrate was originally applied to organic compounds which had a hydrogen:oxygen:carbon ratio of 2:1:1. Today the term carbohydrate applies to a large number of organic compounds, monomeric, oligomeric, and polymeric found in nature, which do not necessarily have the 2:1:1 ratio, but which can be either synthesized from or hydrolyzed to monosaccharides (El Khadem, 1988).

Monosaccharides include two main functional groups, the carbonyl group and the hydroxyl group (**Error! Reference source not found.**). Because of the difference in electronegativity, the carbon-oxygen ond is moderately polar. The polar nature of the carbonyl group controls many of its properties and interactions in materials. The carbonyl group is more polar than the C-O group in an alcohol or ether (Fessenden and Fessenden, 1990). The carbonyl group is reactive due to the difference in electronegativity between the carbon and the oxygen atoms. If the carbonyl group is on the terminal carbon in the monosaccharide, it is an aldehyde; if it occurs on one of the other carbons, it is a ketone (**Error! Reference source not found.**). When the carbonyl group is on the same carbon as the hydroxyl roup, it creates a new functional group called a carboxylic acid. Xylose and glucose are aldehydes; fructose is a ketone. The carboxylic acid has the carbonyl attached to a carbon which is also attached to a hydroxyl group (OH). Citric acid is an example of a material with a carboxylic acid group. Polyols do not possess this carbonyl group; on polyols the carbonyl group has been reduced to a hydroxyl group.

Other common functional groups that contain a carbonyl are found in **Error! Reference source not ound.** (Agvateesiri, 2015).

The carbonyl group is subject to many reactions. Typical bond energy of the carbonyl group is 160 kcal/mole and length 1.20Å (Berthier and Serre, 2010). In aldehydes and ketones, the carbonyl group can be readily oxidized to the corresponding hydroxyl. The autoxidation generally continues through a chain reaction. It is catalyzed by metal ions like iron or cobalt. The initial ions can also come from heat, light or ionizing radiation (Ogata and Kawasaki, 2010). In aldehydes, Glockler (1958) reports the energy of intramolecular hydrogen bonding of 5.0 kcal/mole between the oxygen of the carbonyl group and the adjacent hydrogen. In ketones, Glockler (1958) reports the intramolecular hydrogen bonding energy to be about 3.1 kcal/mole. The bond length of these hydrogen bonding interactions was found to be 2.0 Å. The physicochemical properties of carbonyl compounds with aldehydes and ketones are found to be very homogenous. The oxygen atom in the carbonyl group has two lone electron pairs that contribute to the high electronegativity and reactivity. The carbonyl group is prone to additions and nucleophilic attack because of the polarity of the covalent bond. The carbonyl group is stabilized by adjacent alkyl groups, which are electron releasing. A ketone with two R-groups, is about 7 kcal/mol more stable than an aldehyde with only 1 R-group (Fessenden and Fessenden, 1990). The carbonyl group is important group in the chemistry of mono- and di-saccharides.

The loss of a water molecule in sugars can occur from the action of acids or bases. Aldohexoses are formed by the elimination of a molecule of water between the anomeric hydroxyl group and another hydroxyl group elsewhere in the molecule in dilute acid solutions. The elimination of a water molecule from hydroxyl groups elsewhere in the molecule is known as an anhydro sugar. In acid solutions, the ketones typically form dianhydrides or two fructose molecules with a central dioxane ring. The formation of anhydrides is a clear-cut example of an equilibrium controlled by conformational factors. When the hydroxyl groups are in close proximity, the cleavage of the water molecule is possible (Shallenberger and Birch 1975).

During the heating of an apparent melting material two events occur – melting and thermal decomposition. The isothermal holding of galactose and glucose showed an appearance of initial decomposition components (HMF) at 10% of the time needed for a loss in crystal structure, whereas fructose and xylose showed an increase in decomposition components at the 20%. This indicates that decomposition products can begin to accumulate before enough enthalpy is applied to disrupt the intermolecular bonds.

The decomposition reactions lead to the development of brown color and many highly flavored compounds. In the case of breads and caramels, these reactions and products are desirable. In the case of hard candies or in some sugars, these reactions are undesirable. Understanding when and how these decomposition reactions occur in sugars can be crucial to ensuring high quality food products.

Future Work

1. Complete further investigation of citric acid; determine conclusively if it is thermodynamic or apparent melting.
    - It is proposed to do a pinhole quasi-isothermal experiment that will allow the loss of volatiles, which will affect the weight of the pan and the heat capacity. Monitoring the loss of volatiles caused during decomposition will show when decomposition occurs in relation to the loss in crystal structure.
2. Complete further work on other disaccharides (specifically lactose and mannose) to determine their thermal behavior and how it compares to sucrose and the monosaccharides studied.
    - Do the other disaccharides exhibit two separate peaks under any circumstances?
3. Demonstrate and compare the kinetics of these decomposition reactions.
    - Is there a difference between mono and disaccharides; is there a difference between different monosaccharides?
4. Study other similar carbohydrate compounds with carbonyl groups (e.g. esters, amides, acyl halides) to determine if they are apparent melting or thermodynamic melting materials.
5. Understand the mechanisms which contribute to the early onset decomposition (e.g. carbonyl group, anhydride formation).

Conclusions

The carbonyl groups present in the sugars and not present in the polyols are the common group that seems be present in molecules that exhibit apparent melting. Sugars are susceptible to the formation of anhydrides due to conformational factors. Understanding the factors that influence apparent melting will help predict other compounds that exhibit these thermal characteristics. As we continue to use sugars as a backbone to our food industry, it is important to understand the reactions they undergo. A new trend in the food industry is to consider adding rare sugars (such as ribose or allulose) as a lower calorie functional equivalent to traditional sucrose. Understanding that these sugars

can decompose at temperatures below their melting temperature can lead to better usage of these sugars in processing, resulting in many varied and important foods, both now and in the future.

Figures and Tables Chapter 6

Figure 6-1: Carbonyl and hydroxyl group

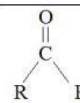
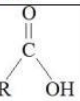
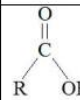
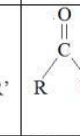
Compound	Aldehyde	Ketone	Formaldehyde	Carboxylic Acid	Ester	Amide	Enone	Acyl Halide	Acid Anhydride
Structure									
General Formula	RCHO	RCOR'	CH2O	RCOOH	RCOOR'	RCONR'R"	RC(O)C(R')CR"R"'	RCOX	(RCO)2O

Figure 6-2: Summary of common functional groups that include the carbonyl group adapted from Agvateesiri (2015)

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Appendix A

Table A-1: Reversing Cp versus hold time of Sigma Sucrose at 132°C from Figure 5-6

Time in Minutes	Reversing Cp J/g°C	Standard Deviation
96	2.25	0.55
192	2.19	0.27
240	2.22	0.46
480	2.54	0.15
720	2.75	0.15
960	3.12	0.47
1920	3.48	0.09

Table A-2: Reversing Cp versus hold time of Fructose at 101°C from Figure 5-9

Time in Minutes	Reversing Cp J/g°C	Standard Deviation
13.5	2.463	0.22
27	2.719	0.09
33.75	2.755	0.04
67.5	2.904	0.66
101.25	2.904	0.36
135	2.795	0.77
270	3.083	0.26

Table A-3: Reversing Cp versus hold time of Galactose at 151°C from Figure 5-12

Time in Minutes	Reversing Cp J/g°C	Standard Deviation
15.5	1.97	0.15
31	1.98	0.24
38.75	2.09	0.12
77.5	2.12	0.21
116.25	1.99	
155	2.97	0.46
310	3.19	0.33

Table A-4: Reversing Cp versus hold time of Glucose monohydrate at 140°C from Figure 5-15

Time in Minutes	Reversing Cp J/g°C	Standard Deviation
11	1.73	0.42
22	1.97	0.41
27.5	2.10	0.42
55	2.24	0.10
82.5	2.83	0.20
110	3.40	0.17
220	3.12	0.20

Table A-5: Reversing Cp versus hold time of xylose at 132°C from Figure 5-18

Time in Minutes	Reversing Cp J/g°C	Standard deviation
13.50	1.93	0.25
27.00	1.91	0.34
33.75	2.24	0.06
67.50	2.42	0.31
101.25	2.66	0.09
135.00	2.95	0.07
270.00	3.26	0.19

Table A-6: Glucose, Fructose, Sucrose, HMF and Furfural in Sigma Sucrose held at 132°C from Figure 5-7

Time in minutes	Glucose %	standard deviation	Fructose %	standard deviation	Sucrose %	standard deviation	HMF (ppm)	standard deviation	Furfural (ppm)	standard deviation
0.00	0.00		0.00		100.00		0.00		0.00	
96.00	1.43	0.04	0.12	0.11	97.99	2.01	100.78	26.41	2.73	1.04
192.00	2.20	0.11	0.18	0.16	95.40	0.60	131.50	12.23	3.97	1.16
240.00	2.86	0.34	0.22	0.19	95.09	0.91	157.02	71.71	4.31	1.54
480.00	8.50	2.01	0.75	0.71	78.78	4.43	1012.85	362.63	29.01	14.89
720.00	24.28	2.38	2.19	2.19	44.10	2.95	3148.93	222.81	120.18	7.30
960.00	31.78	1.73	3.53	3.53	8.77	0.87	8406.75	999.5	485.54	112.23
1920.00	10.59	1.27	2.65	2.65	0.00		17920.21	436.40	1333.98	137.61

Table A-7: Fructose, HMF and Furfural in Fructose samples held at 101°C for various times from Figure 5-10

Time in Minutes	% Fructose	Standard Deviation	HMF (ppm)	Standard Deviation	Furfural (ppm)	Standard Deviation
0.00	100.00	0.05	4.27	0.35	0.07	0.12
13.50	101.21	0.77	4.10	0.29	0.21	0.36
27.00	100.04	8.80	5.84	0.86	0.08	0.13
33.75	101.47	20.32	6.03	1.38	0.00	0.00
67.50	100.05	17.98	12.17	5.17	0.18	0.31
101.25	93.14	17.11	22.17	14.03	0.16	0.27
135.00	75.81	20.34	44.17	19.77	0.12	0.20
270.00	72.83	18.83	656.02	950.14	3.22	5.57

Table A-8: Galactose, HMF and Furfural in Galactose samples held at 151°C for various times from Figure 5-13

Time in Minutes	% Galactose	standard deviation	HMF (ppm)	standard deviation	Furfural (ppm)	standard deviation
0.00	100.00	0.00	0.00	0.00	0.00	0.00
15.50	94.75	2.02	8.24	2.78	0.08	0.14
31.00	103.89	3.76	21.51	7.70	0.08	0.15
38.75	103.12	3.70	24.12	10.91	0.11	0.20
77.50	103.63	3.92	57.31	20.12	0.32	0.56
116.25	98.20	10.22	67.82	44.49	0.30	0.42
155.00	63.74	2.56	150.42	20.94	5.77	1.15
310.00	13.50	1.12	1558.49	261.31	62.13	13.83

Table A-9: Glucose, HMF and Furfural in Glucose monohydrate samples held at 140°C for various times from Figure 5-16

Time in Minutes	% Glucose monohydrate	standard deviation	HMF (ppm)	standard deviation	Furfural (ppm)	standard deviation
0.00	100.00	0.00	0.00	0.00	0.00	0.00
11.00	93.87	8.43	0.35	0.60	0.00	0.00
22.00	92.81	2.50	2.17	2.41	0.00	0.00
27.50	102.73	8.72	4.93	3.39	0.00	0.00
55.00	104.46	1.24	18.61	10.34	0.00	0.00
82.50	96.82	5.08	43.97	16.83	0.00	0.00
110.00	87.16	8.09	54.14	27.62	0.08	0.14
220.00	64.92	4.76	349.85	57.75	15.46	4.30

Table A-10: Xylose and Furfural in Xylose samples held at 132°C for various times from Figure 5-19

Time in Minutes	% Xylose	standard deviation	Furfural (ppm)	standard deviation
0.00	100.00	0.04	0.00	0.00
45.90	95.26	6.57	0.00	0.00
91.80	100.10	3.64	2.77	3.91
114.75	103.02	1.31	6.35	1.15
229.50	100.14	2.77	45.62	5.63
344.25	86.07	14.54	112.94	10.48
459.00	71.64	7.48	211.21	5.70
918.00	38.86	2.40	1168.41	80.88

Table A-11: Xylitol, HMF and Furfural in xylitol samples held at 94°C for various times from Figure 5-22

Time in Minutes	% Xylose	standard deviation	HMF (ppm)	Furfural (ppm)
0.00	100.00	0.04	0.00	0.00
1000	100.00	0.02	0.00	0.00
2000	100.00	0.09	0.00	0.00
3000	100.00	0.04	0.00	0.00

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